

Network Systems
Science & Advanced
Computing
Biocomplexity Institute
& Initiative
University of Virginia

Estimation of COVID-19 Impact in Virginia

August 4th, 2021

(data current to July 25th – 27th)

Biocomplexity Institute Technical report: TR 2021-086



BIOCOMPLEXITY INSTITUTE

biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



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Overview

- **Goal:** Understand impact of COVID-19 mitigations in Virginia
- **Approach:**
 - Calibrate explanatory mechanistic model to observed cases
 - Project based on scenarios for next 4 months
 - Consider a range of possible mitigation effects in "what-if" scenarios
- **Outcomes:**
 - Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
 - Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.

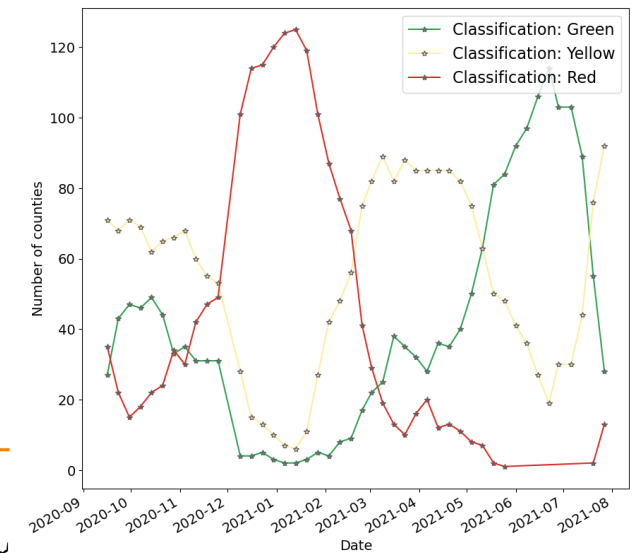
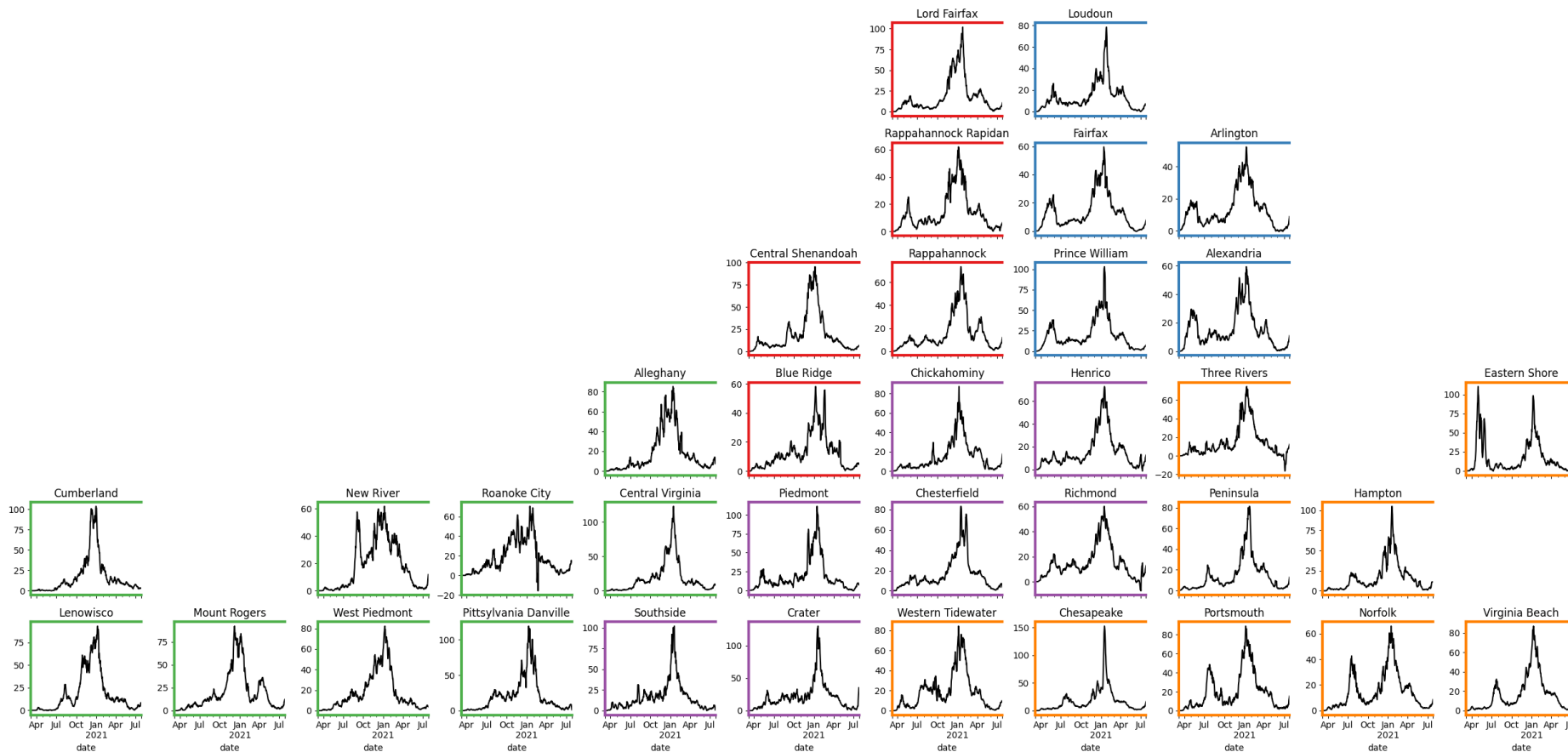
Even without perfect projections, we can confidently draw conclusions:

- **Case rates in Virginia continue to rise quickly amidst a background of surges across the nation**
- VA mean weekly incidence up to 14/100K from 7.8/100K, US up to 25/100K (from 15.6/100K)
- Vaccination rates continue rebound while acceptance among the unvaccinated ticks up and mask usage also increases slightly
- Uncertainty around severity of Delta variant remains, however, the experience of other states / countries suggest potential for higher severity
- Recent updates:
 - Analysis of mask use, reasons by vax acceptance level
 - Deeper dive on Delta variant severity

The situation continues to change. Models continue to be updated regularly.

Situation Assessment

Case Rates (per 100k) and Test Positivity



<https://data.cms.gov/stories/s/q5r5-gjyu>

County level test positivity from RT-PCR tests.

Green: <5.0%

(or with <20 tests in past 14 days)

Yellow: 5.0%-10.0%

(or with <500 tests and <2000 tests/100k and >10% positivity over 14 days)

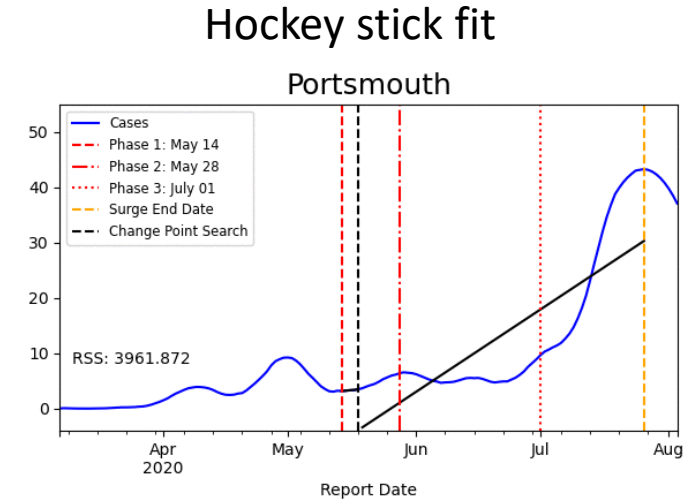
Red: >10.0%

(and not "Green" or "Yellow")

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

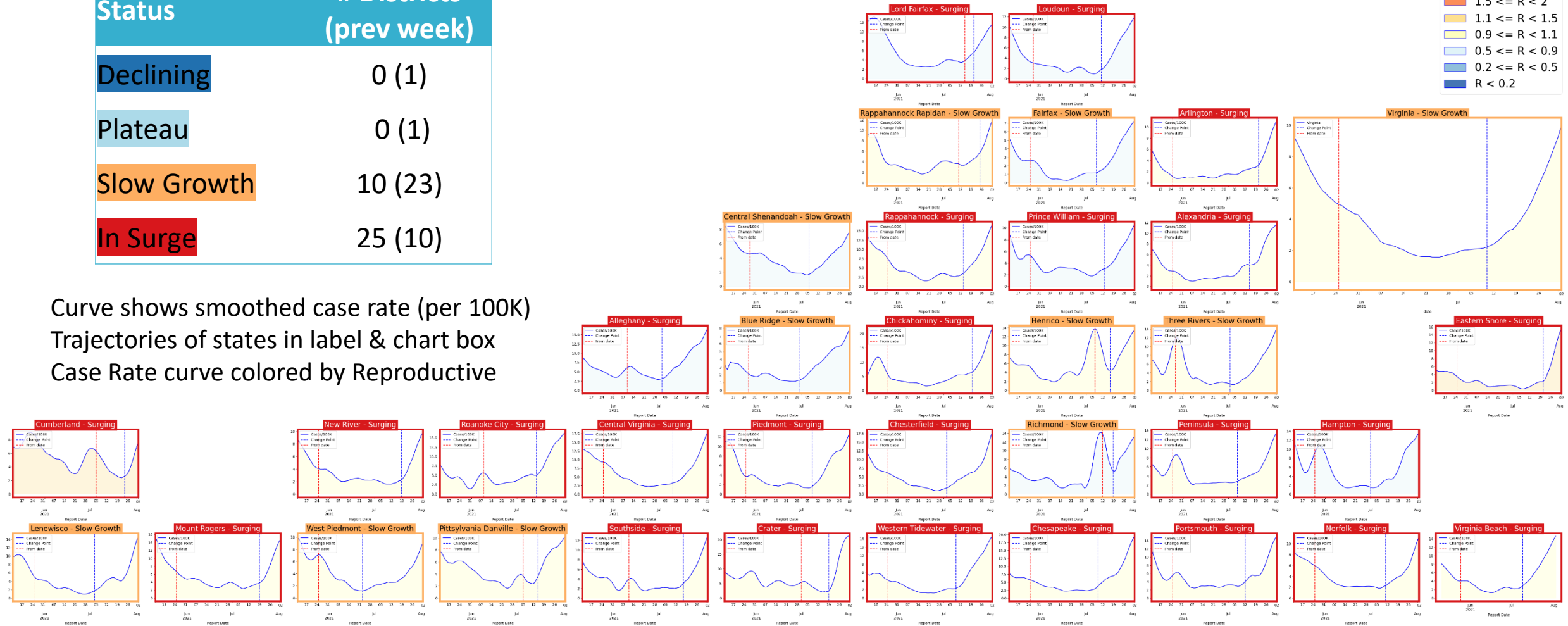


Trajectory	Description	Weekly Case Rate (per 100K) bounds	# Districts (prev week)
Declining	Sustained decreases following a recent peak	below -0.9	0 (1)
Plateau	Steady level with minimal trend up or down	above -0.9 and below 0.5	0 (1)
Slow Growth	Sustained growth not rapid enough to be considered a Surge	above 0.5 and below 2.5	10 (23)
In Surge	Currently experiencing sustained rapid and significant growth	2.5 or greater	25 (10)

District Trajectories – last 10 weeks

Status	# Districts (prev week)
Declining	0 (1)
Plateau	0 (1)
Slow Growth	10 (23)
In Surge	25 (10)

Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive



Estimating Daily Reproductive Number

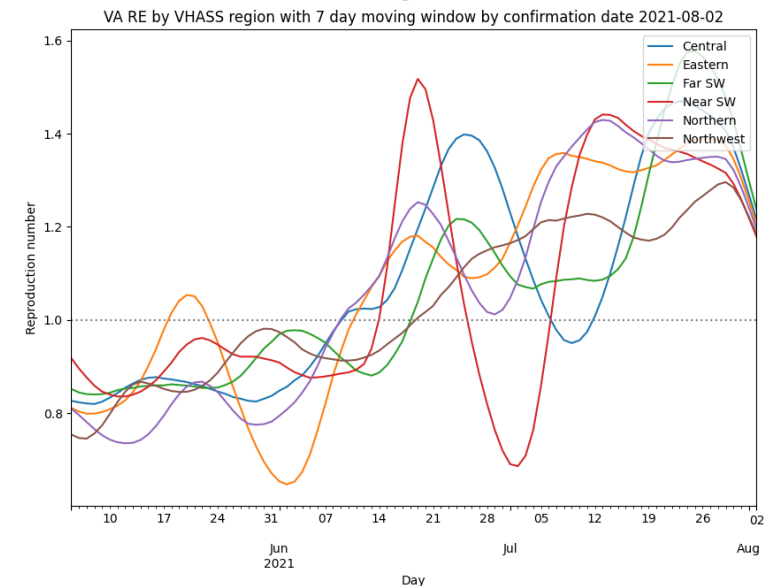
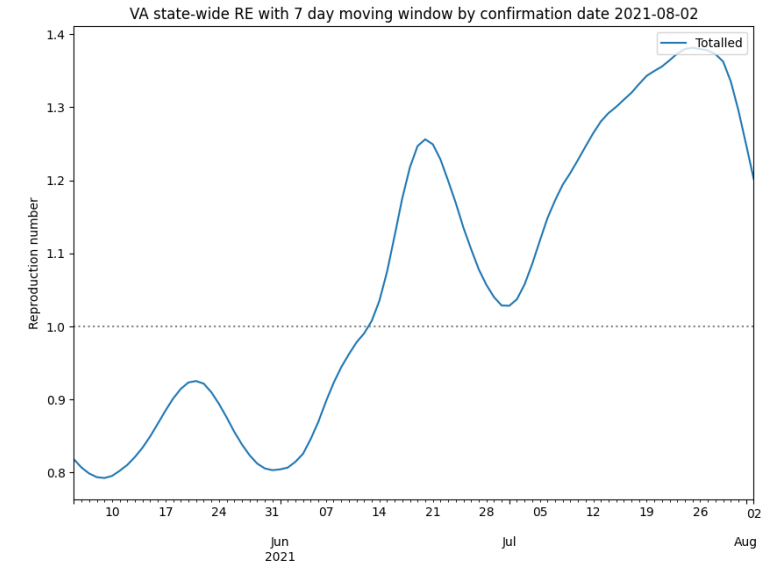
August 2nd Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide	1.202	0.009
Central	1.216	-0.015
Eastern	1.206	0.016
Far SW	1.237	0.027
Near SW	1.179	-0.002
Northern	1.196	0.002
Northwest	1.184	0.058

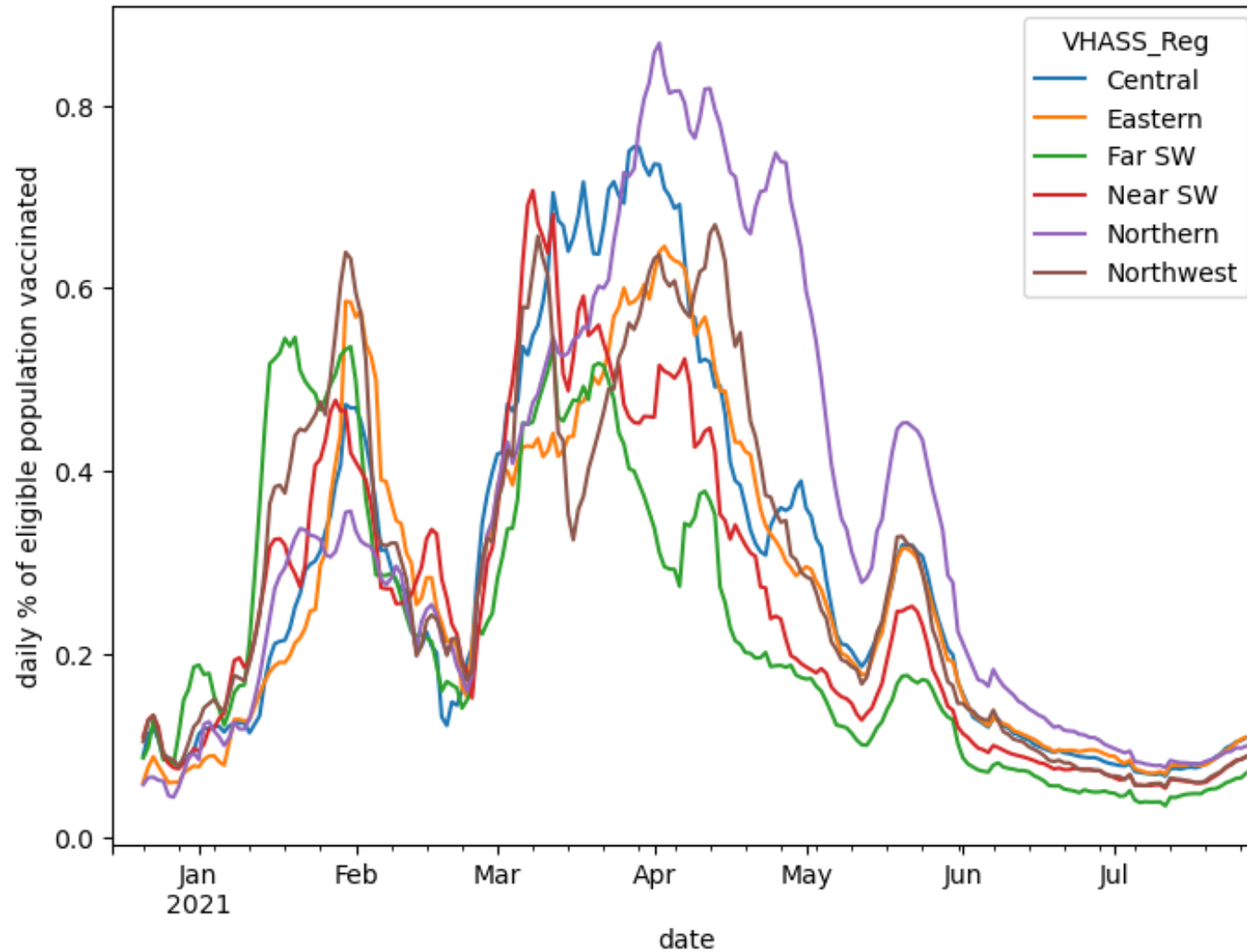
Methodology

- Wallinga-Teunis method (EpiEstim¹) for cases by confirmation date
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

1. Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, <https://doi.org/10.1093/aje/kwt133>

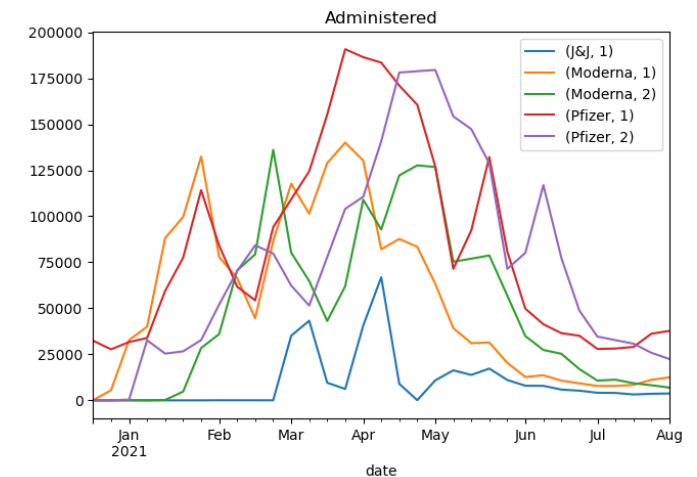


Vaccination Administration Continues Slow Rise

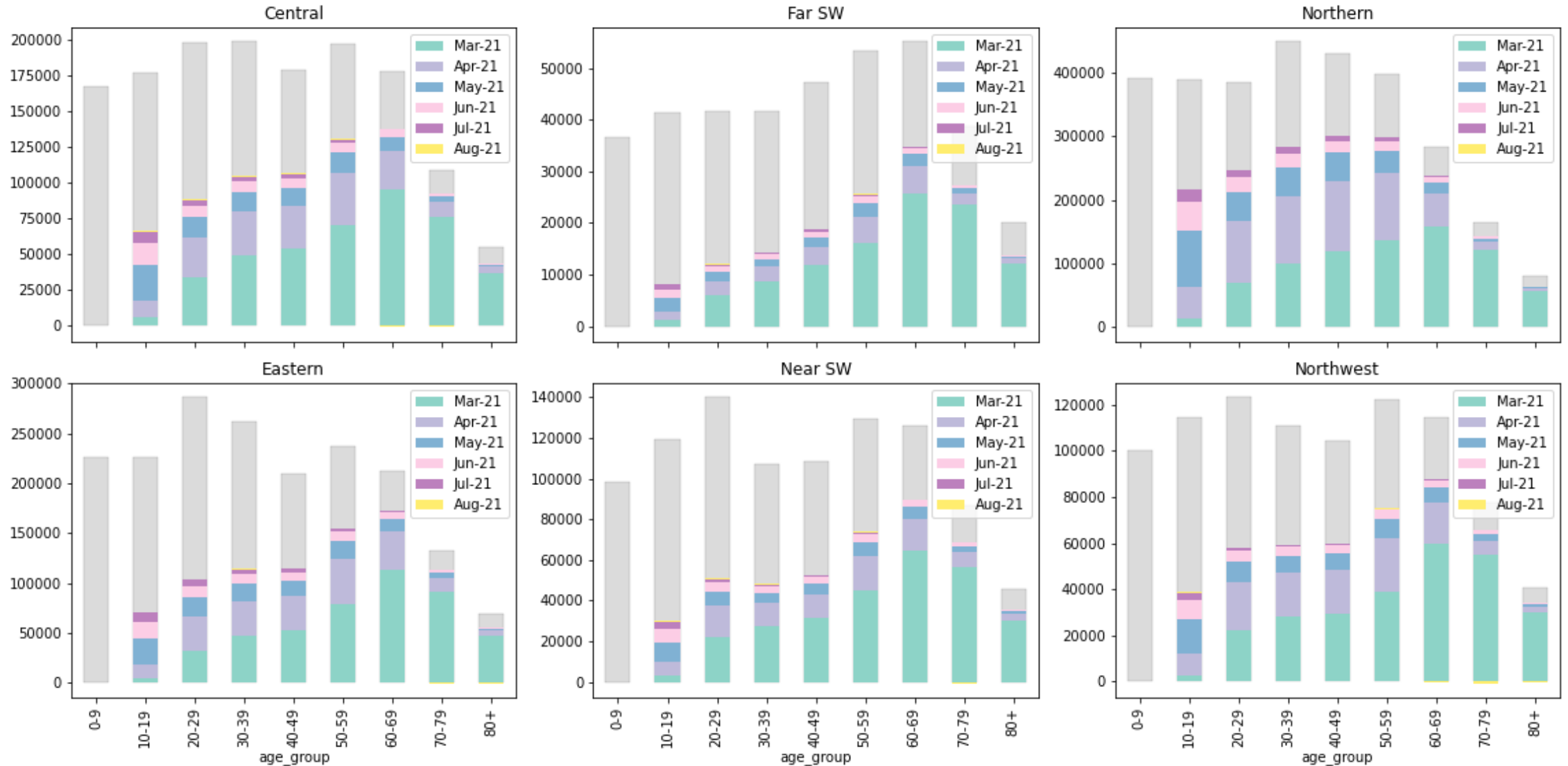


Regional Vaccine courses initiated per day per capita:

- Total counts of first dose of vaccines across regions
- Very slight rise across all regions
- Reflected in 1st dose of Pfizer and Moderna uptick



Vaccinations Shift to Younger Populations

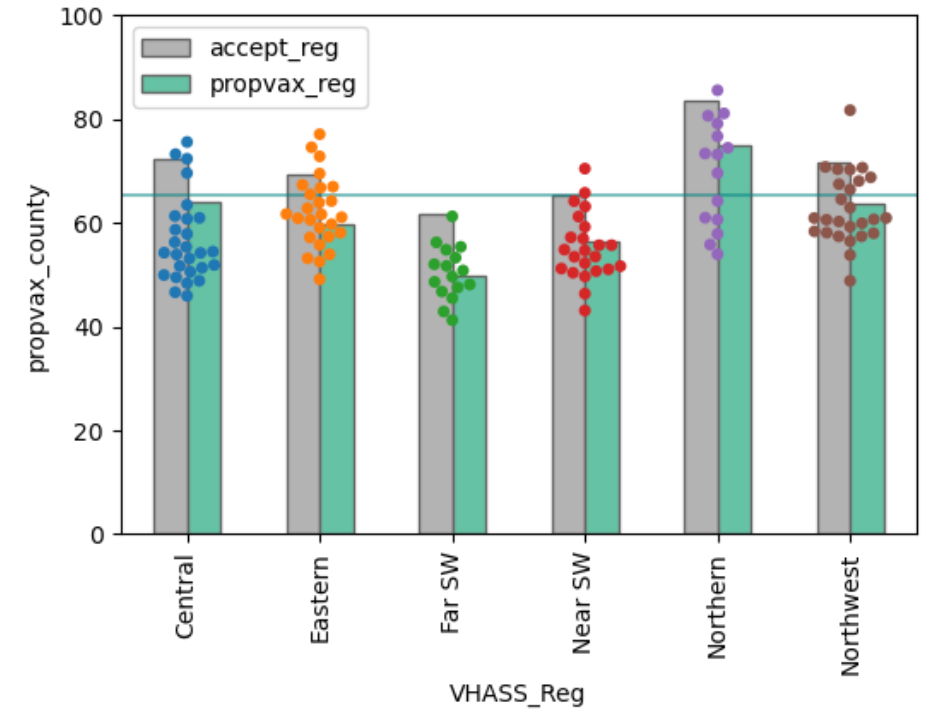


Vaccination Acceptance by Region

Corrections to surveys:

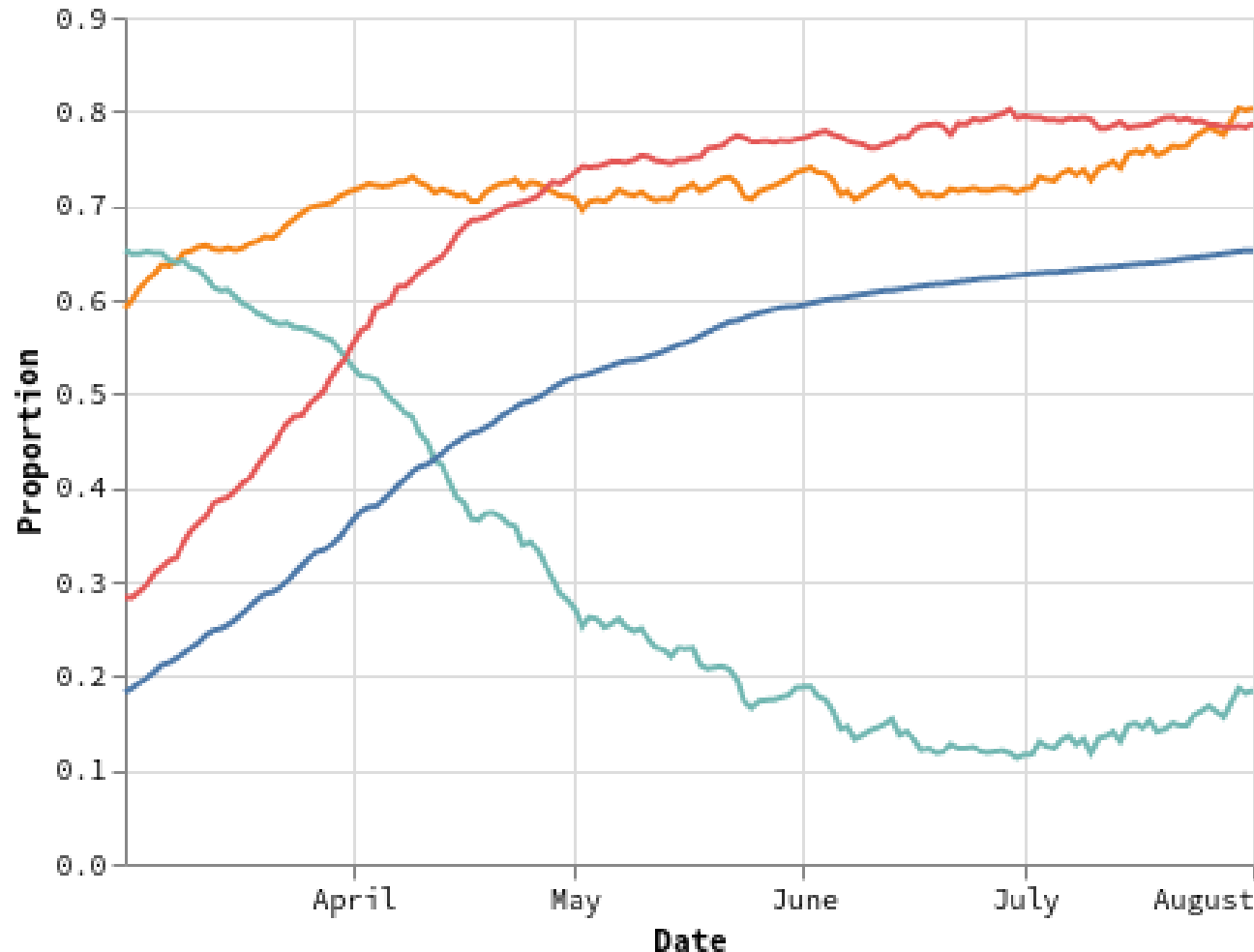
- Facebook administered survey is timely and broad, but biased by who accesses Facebook and answers the survey
- Correction approach:
 - Calculate an over-reporting fraction based on reported vaccinations compared to VDH administration data
 - Cross-validate coarse corrections against HPS survey at the state level and corrected in same manner

Region	COVIDcast accepting corrected	VDH proportion eligible vaccinated
Central	77%	64%
Eastern	74%	60%
Far SW	62%	50%
Near SW	69%	56%
Northern	100%	75%
Northwest	73%	64%
Virginia	80%	65%



Grey Bar: Survey measured and corrected acceptance
Green Bar: Proportion of eligible population administered a vaccine
Dots: Proportion administered at least one dose for each county

Vaccine Acceptance Components over Time



variable

- Administered Vaccines
- Corrected Acceptance
- Surveyed Vaccinated
- Unvaccinated Acceptance

Vaccine Acceptance has risen as vaccination rates have climbed

- Corrected Acceptance reflects the daily measured overall acceptance and has risen in the past couple days
- Unvaccinated Acceptance shows still ~10% of those who are unvaccinated are definitely or probably willing to be vaccinated
- Unvax acceptance has declined a bit and leveled off in last couple of weeks, final 10% may be waiting for FDA approval

Data Source: <https://covidcast.cmu.edu>

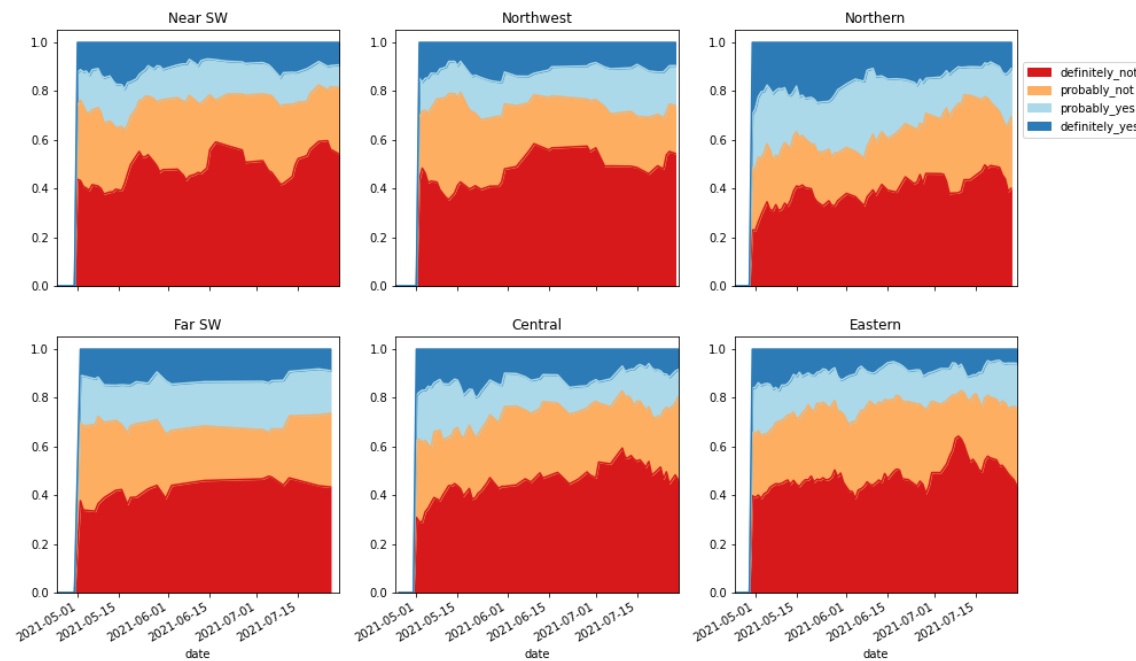
6-Aug-21

Vaccine Acceptance by Region- COVIDcast

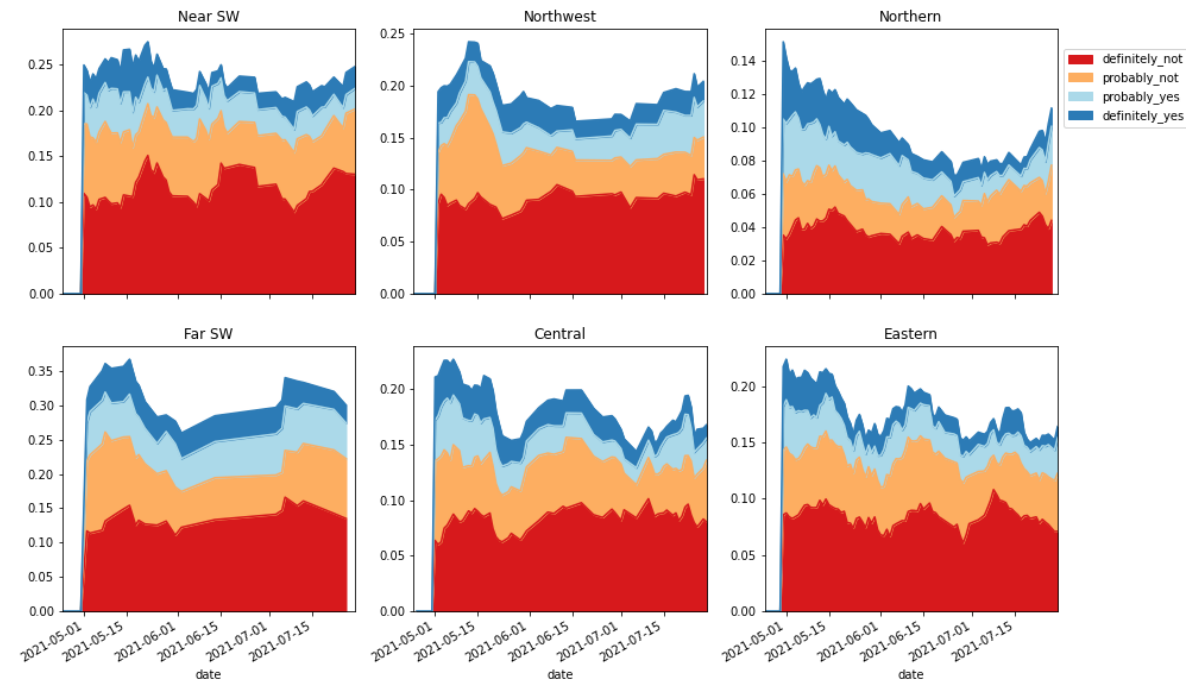
Levels of Acceptance and potential acceptance in flux:

- Nearly all the “definitely yes” have been vaccinated, yet there are 10-15% remaining across the regions
- Northwest and Southwest (to lesser degree) see growth in “probably not”, seemingly from “definitely not”

Unvaccinated Only



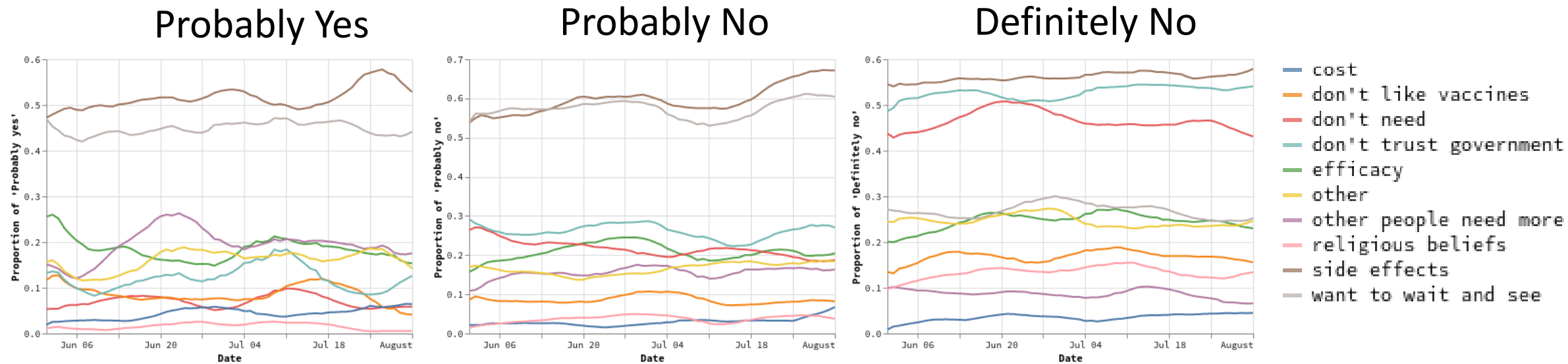
All Respondents



Data Source: <https://covidcast.cmu.edu>

6-Aug-21

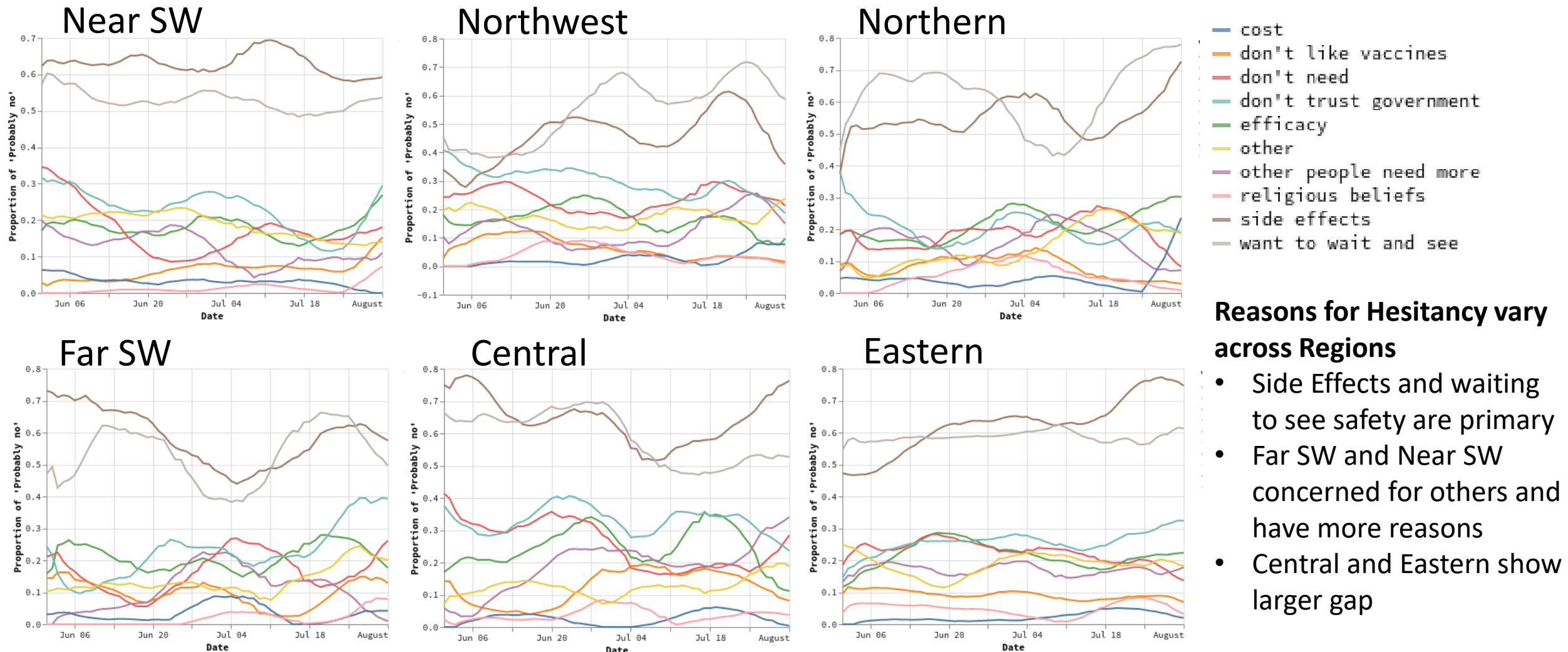
Reasons for Hesitancy by Likelihood to Accept



Reasons for Hesitancy vary across tiers of likelihood to accept the vaccine

- Probably Yes and Probably No most concerned about side effects & are waiting to see
- Definitely No are concerned about side effects but also don't think they need the vaccine and don't trust the government
- Most other reasons are below 30% within these tiers of likelihood

Reasons for Hesitancy (probably no) by Region



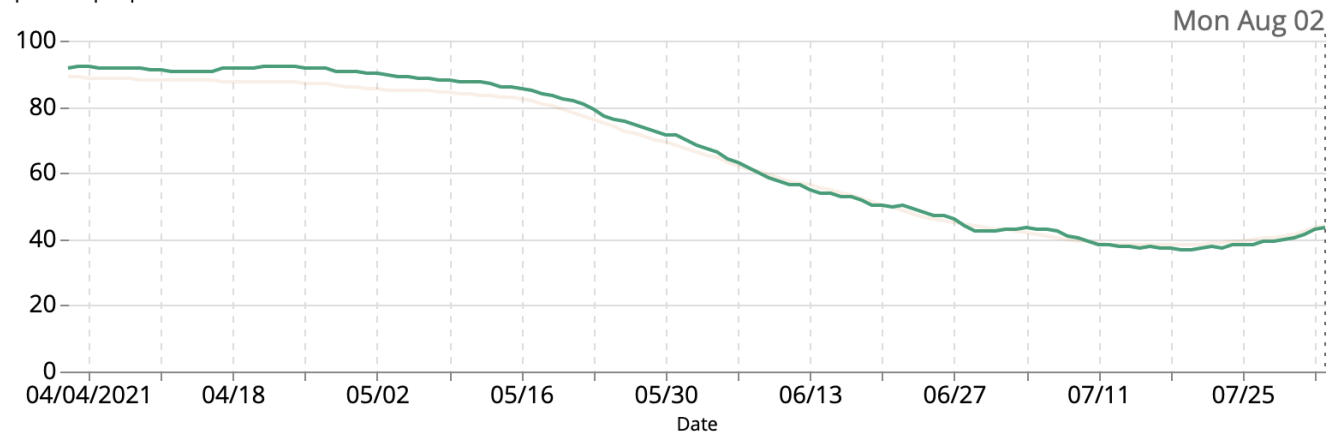
Mask Usage Increases Slightly

Self-reported mask usage has declined for months, but rebounded

- State-wide up to 43% from low 37%, similar to US overall
- Uptick experienced in most counties across VA

PEOPLE WEARING MASKS CHART

People Wearing Masks in Virginia
per 100 people



☐ Rescale Y-axis ☐ Show All Dates

● Virginia
43.50% per 100

● United States
43.86% per 100

Data Source: <https://covidcast.cmu.edu>

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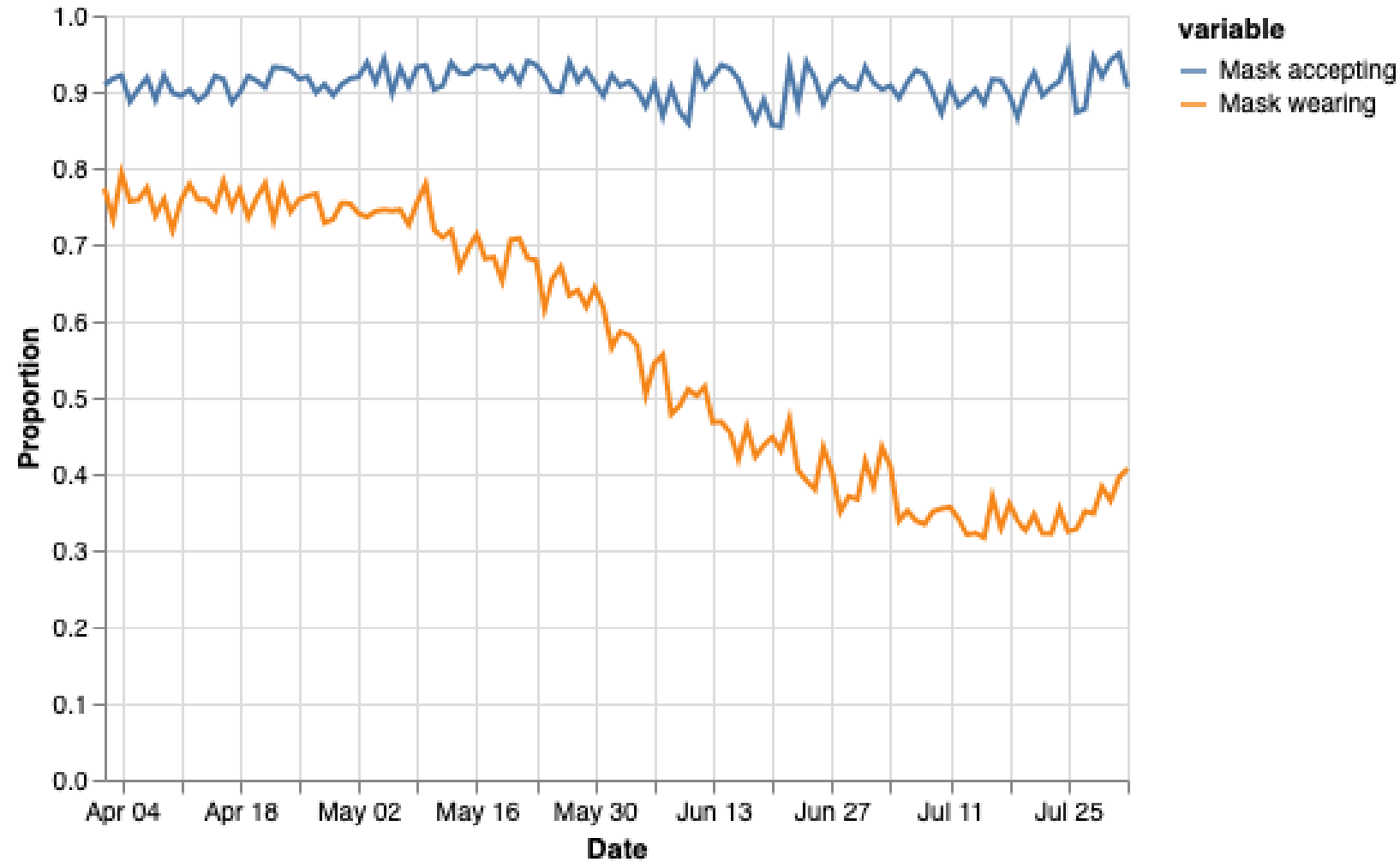
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Virginia Beach, VA	↑ +29.25%	31.98% /100	
Newport News, VA	▲ +100.00%	34.98% /100	
Chesterfield County, VA	↓ -25.35%	35.20% /100	
Chesapeake, VA	↓ -15.16%	35.53% /100	
Arlington County, VA	▲ +100.00%	39.42% /100	
Loudoun County, VA	↑ +12.29%	41.76% /100	
Henrico County, VA	↓ -13.70%	42.30% /100	
Norfolk, VA	↓ -2.57%	43.65% /100	
Richmond, VA	↓ -7.13%	48.15% /100	
Fairfax, VA	↑ +1.10%	51.58% /100	
Prince William County, VA	↓ -4.23%	57.84% /100	

Vax Acceptance is High among Mask Wearers

Self-reported mask usage in Virginia

- Of those who do wear a mask most of the time, 90% are vaccine accepting



Data Source: <https://covidcast.cmu.edu>

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SARS-CoV2 Variants of Concern

Emerging new variants will alter the future trajectories of pandemic and have implications for future control

- Emerging variants can:
 - Increase transmissibility
 - Increase severity (more hospitalizations and/or deaths)
 - Limit immunity provided by prior infection and vaccinations
- Genomic surveillance remains very limited
 - Challenges ability to estimate impact in US to date and estimation of arrival and potential impact in future

	New WHO Name	Transmissibility	Immune Evasiveness	Vaccine Effectiveness [^]
Ancestral		—	—	✓
D614G		+	—	✓
B.1.1.7	Alpha	+++	—	✓
B.1.351	Beta	+	++++	✓
P.1	Gamma	++	++	✓
B.1.429	Epsilon	+	+	✓
B.1.526	Iota	++	+	✓
B.1.617.2	Delta	++++*	++ [#]	✓

[^]Relative transmissibility to B.1.1.7 yet to be fully defined

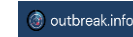
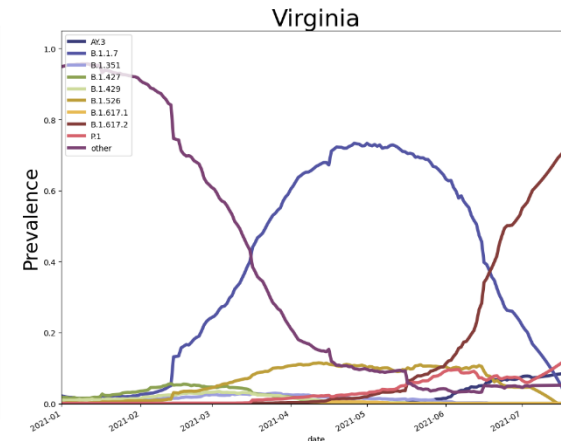
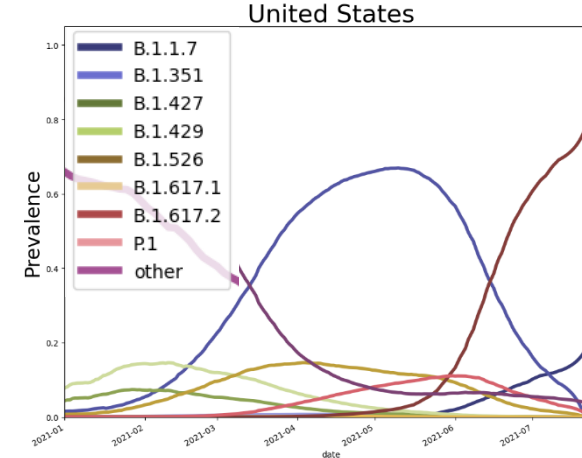
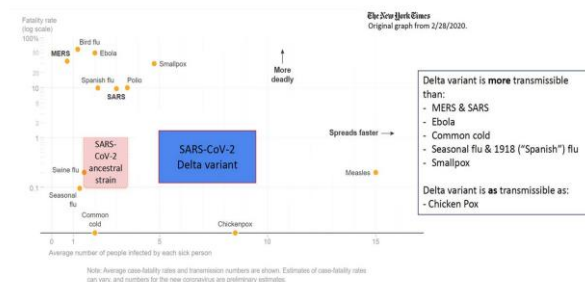
[#]Effectiveness from real world evidence vs. severe illness, not all vaccines are effective vs all variants, and importance of 2-doses, especially for B.1.617.2 for which 1 dose of mRNA or AZ is only ~30% effective [#] May carry more immune escape than P.1, to be determined



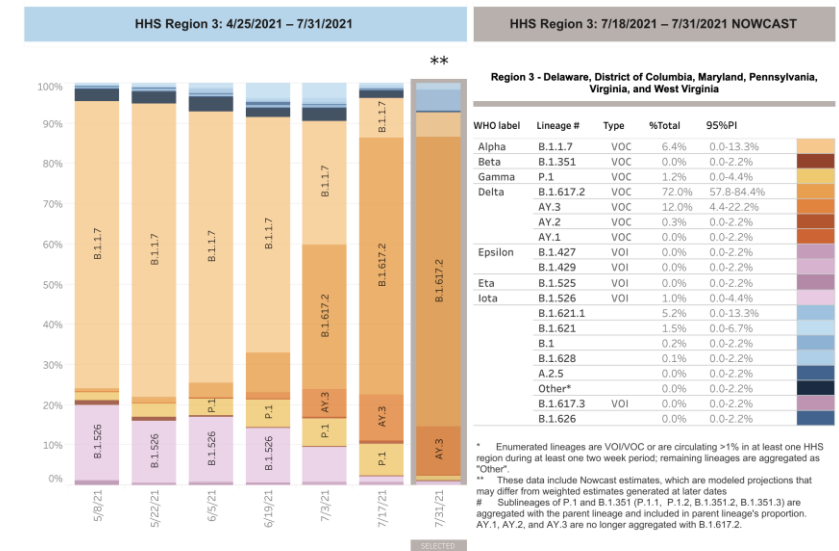
World Health Organization

WHO and Eric Topol

Transmission of Delta variant vs. ancestral strain and other infectious diseases



[Outbreak Info](https://www.outbreak.info)



* Enumerated lineages are VOI/VOC or are circulating >1% in at least one HHS region during at least one two week period; remaining lineages are aggregated as "Other".
 ** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates.
 # Sublineages of P.1 and B.1.351 (P.1.1, P.1.2, B.1.351.2, B.1.351.3) are aggregated with the parent lineage and included in parent lineage's proportion. AY.1, AY.2, and AY.3 are no longer aggregated with B.1.617.2.

Collection date, two weeks ending



CDC Variant Tracking

SARS-CoV2 Variants of Concern

Alpha α - Lineage B.1.1.7

Prevalence: Levels have stalled and are now dropping in most states; flat in VA

Transmissibility: Estimated increase of 50% compared to previous variants. B.1.1.7's mutations boost its overall levels of viremia; [study from Public Health England](#) shows contacts of B.1.1.7 cases are more likely (50%) to test positive

Severity: Increased risk of hospitalization (60%) and mortality (60%). [Danish](#) study shows B.1.1.7 to have a 64% higher risk of hospitalization, while [Public Health Scotland](#) studies showed a range of 40% to 60%; [Study in Nature](#) estimates 60% higher mortality

Beta β - Lineage B.1.351

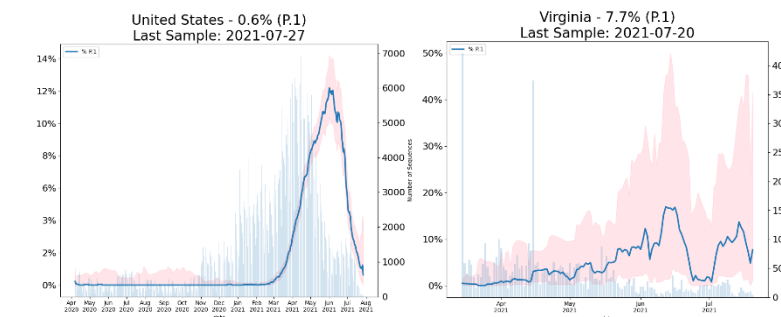
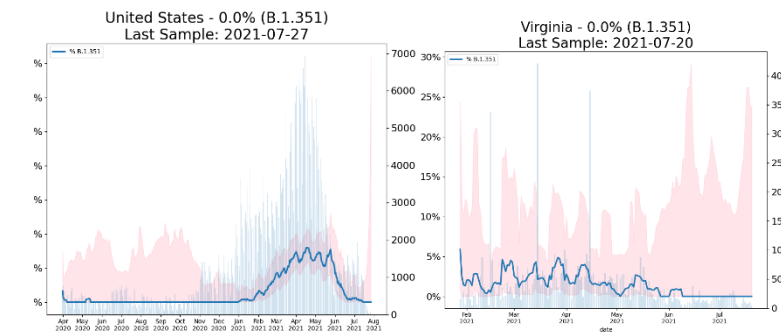
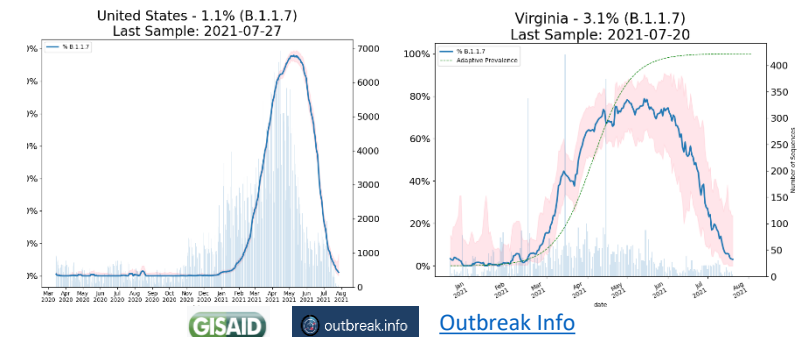
Prevalence: Levels have remained low, as this variant's transmissibility can't compete with B.1.1.7, however, as more of the population becomes immune it may gain an advantage

Immune Escape: Many studies show that convalescent sera from previously infected individuals does not neutralize B.1.351 virus well which is [predictive](#) of [protection](#), however, [vaccine induced immunity](#) shows [signs](#) of [effectiveness](#)

Gamma γ - Lineage P.1

Prevalence: Nationally at 10%, slow increase in VA at 9%

[Study](#) estimates 17-32% of all infections in Manaus in 2021 were reinfections, which helps explain [data from Brazil](#) demonstrating P.1's continued dominance in Rio despite presence of B.1.1.7



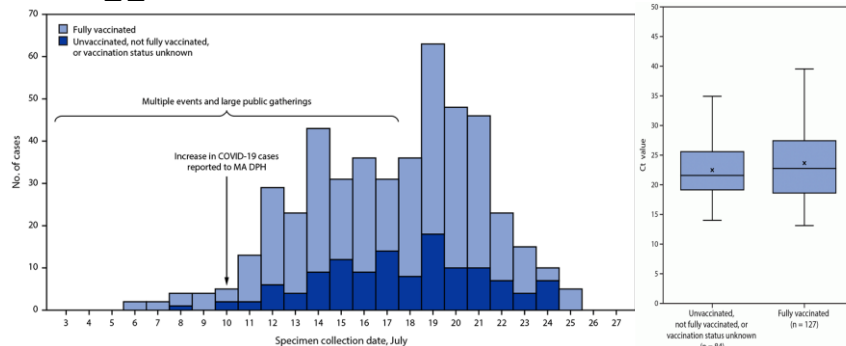
SARS-CoV2 Variants of Concern

Delta δ - Lineage B.1.617.2 and related subvariants

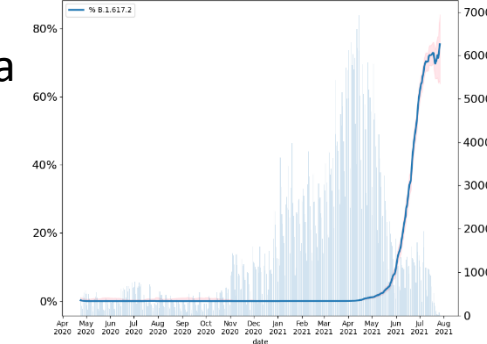
- Delta plus $\delta+$ lineage which contains the K417N mutation is emerging as a sub-variant that is even more transmissible; declared a VoC in India
- Delta variant now dominates most of Europe and US
- CDC recommends resumption of mask wearing indoors due to reports of breakthrough infections of the vaccinated possibly being transmissible
- [More reports](#) describe time Delta variant escapes vaccine immunity, with [recent Israeli study](#) showing a 64% efficacy against infection, however, remains highly effective against hospitalization and death
- [Public Health Scotland study in Lancet](#) suggests Delta is 2x more likely to cause hospitalization than Alpha
- Subvariant AY.3 of Delta is increasingly prevalent and arose in US, may be more transmissible than Delta itself, though some fitting studies suggest otherwise

Fully vaccinated breakthrough cluster in Barnstable County, Massachusetts, July 2021. Ct values only marginally higher in vaccinated individuals
[CDC MMWR](#)

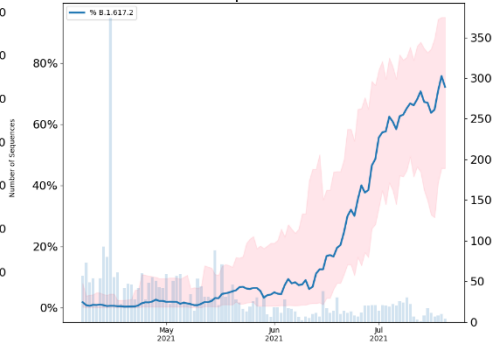
6-Aug-21



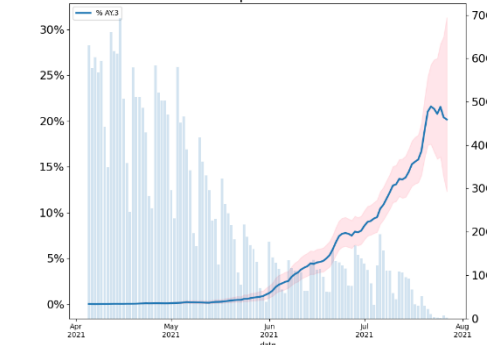
United States - 75.4% (B.1.617.2)
Last Sample: 2021-07-27



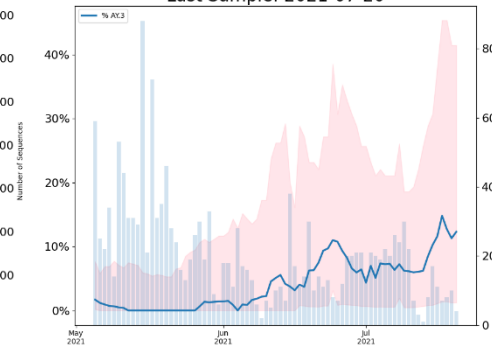
Virginia - 72.3% (B.1.617.2)
Last Sample: 2021-07-20



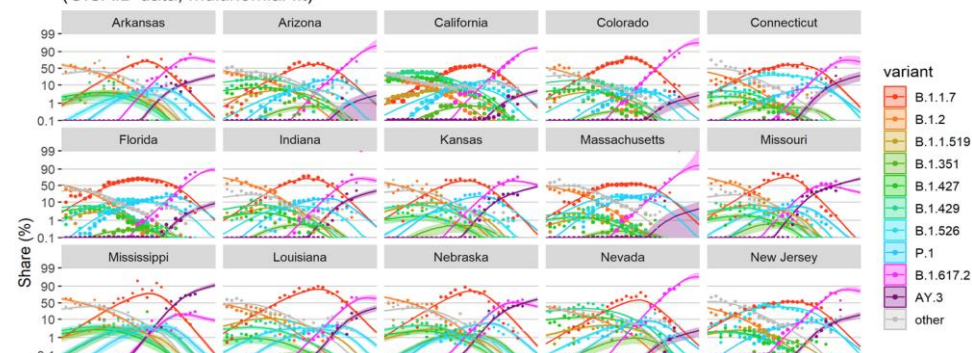
United States - 20.2% (AY.3)
Last Sample: 2021-07-27



Virginia - 12.3% (AY.3)
Last Sample: 2021-07-20

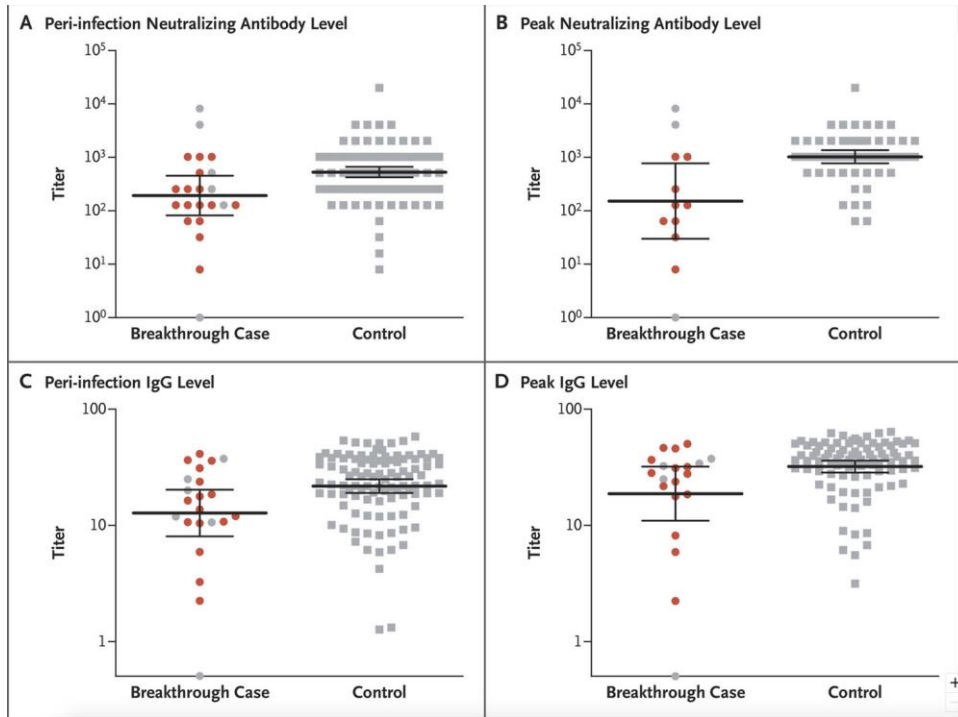


SPREAD OF SARS-CoV2 VARIANTS OF CONCERN IN THE USA
(GISAID data, multinomial fit)

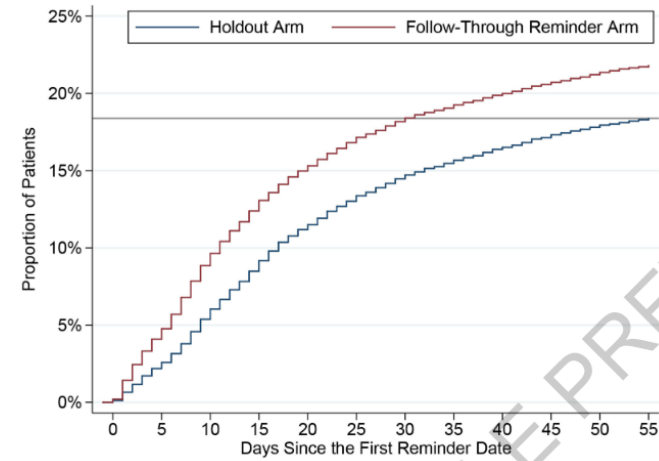


Recent multinomial fits appear to show no growth advantage of AY.3 over other Delta substrains [Twitter](#)

SARS-CoV2 Variants and Vaccine



Among 1497 fully vaccinated health care workers for whom RT-PCR data were available, **39 SARS-CoV-2 breakthrough infections were documented**. Neutralizing antibody titers in vaccinated break through infections during the peri-infection period were lower than those in matched uninfected controls (case-to-control ratio, 0.361; 95% confidence interval, 0.165 to 0.787). Higher peri-infection neutralizing antibody titers were associated with lower infectivity (higher Ct values).
https://www.nejm.org/doi/full/10.1056/NEJMoa2109072?query=feature_d_home



Behavioral Nudges Increase COVID-19 Vaccinations

<https://www.nature.com/articles/s41586-021-03843-2>

If You Got the Johnson & Johnson Shot, SF General Will Give You a 'Supplemental' Pfizer or Moderna Shot

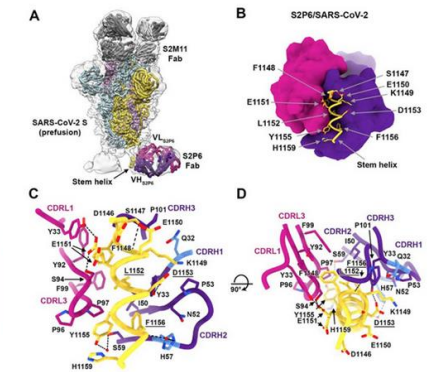
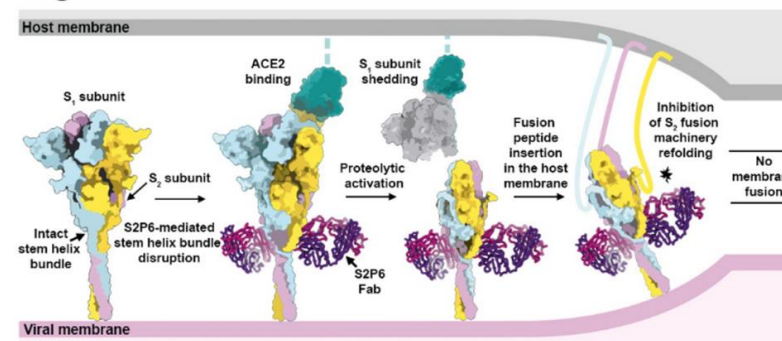
Starting later this week, if you received the one-shot Johnson & Johnson vaccine, you're eligible to drop into the vaccination clinic at SF General and get a "supplemental" mRNA vaccine dose — but don't call it a booster.

The decision was made Monday by Zuckerberg San Francisco General Hospital (ZSFG) and San Francisco's Department of Public Health (SFDPH), as **ABC 7 reports**, following multiple reports that the J&J vaccine may not be as effective in preventing infection from the Delta variant as mRNA-based Pfizer and Moderna vaccines. With the first variants of COVID-19 that were spreading last year, the J&J vaccine was seen as highly effective in preventing severe illness, but new data suggests that the mRNA vaccines provide strong protection against what appears to be a stronger and more infectious variant.

But they are being careful to call it a "supplemental dose," not a booster.

Supplemental mRNA vaccines for those who originally got J&J offered in San Francisco
<https://sfist.com/2021/08/03/if-you-got-the-johnson-johnson-shot-sf-general-will-give-you-a-supplemental/>

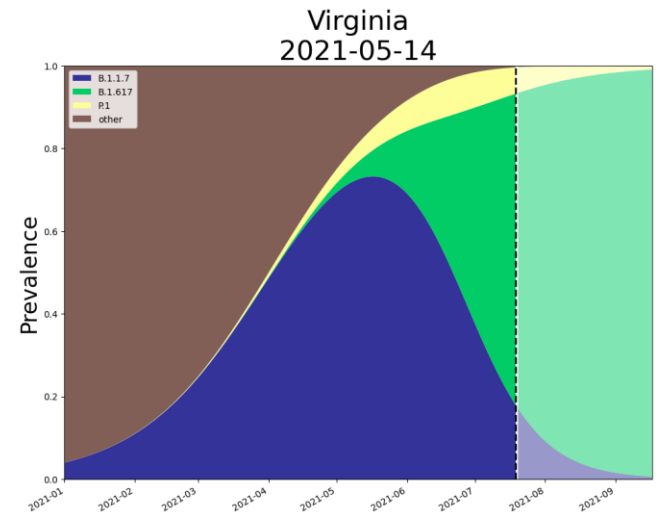
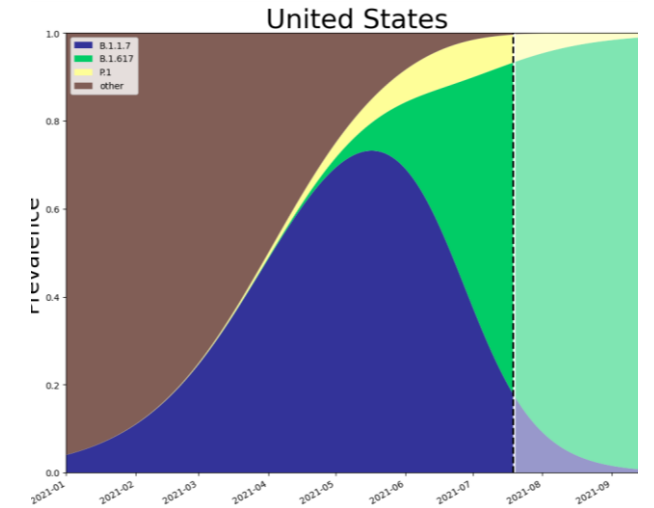
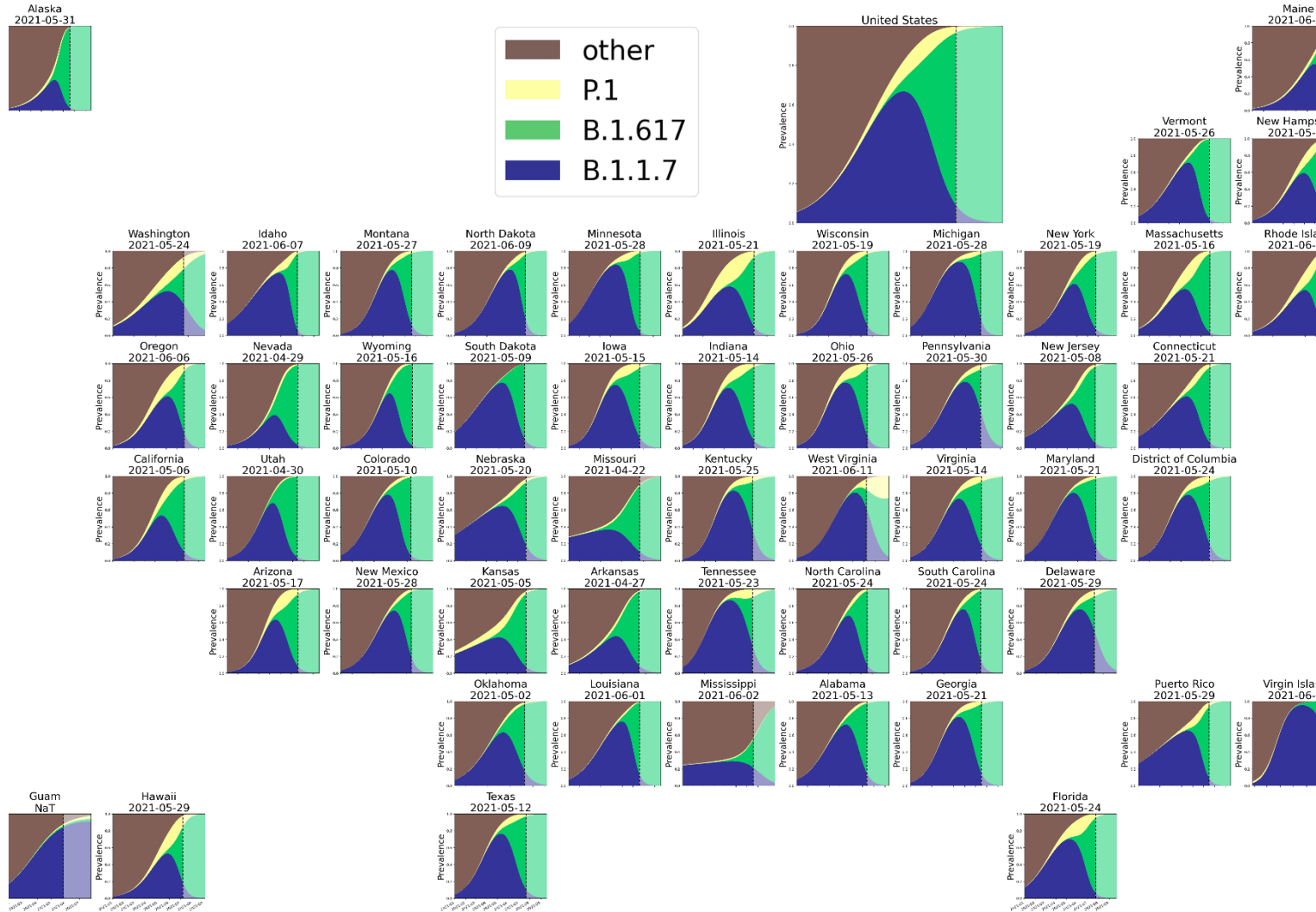
Broad betacoronavirus neutralization by a stem helix-specific human antibody



Potential for universal betacoronavirus vaccine

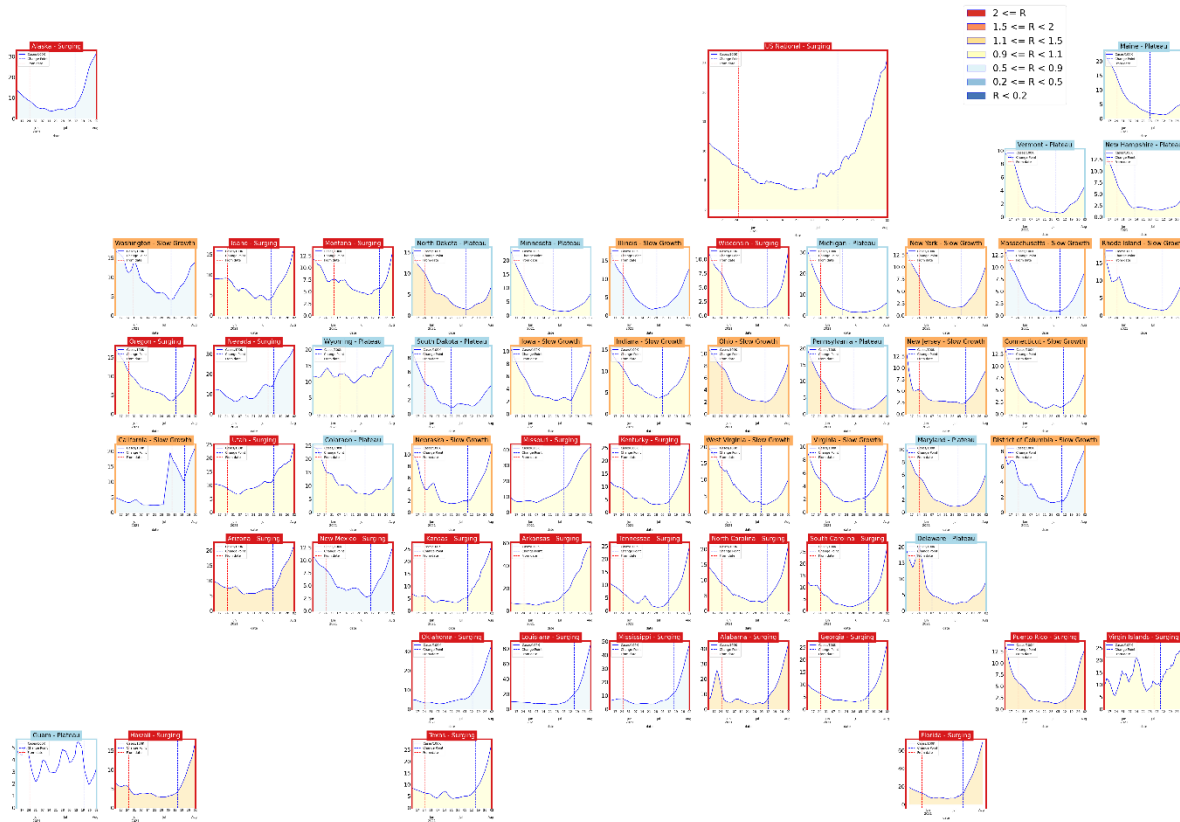
<https://science.sciencemag.org/content/early/2021/08/03/science.abj3321>


Variant of Concern Trajectories



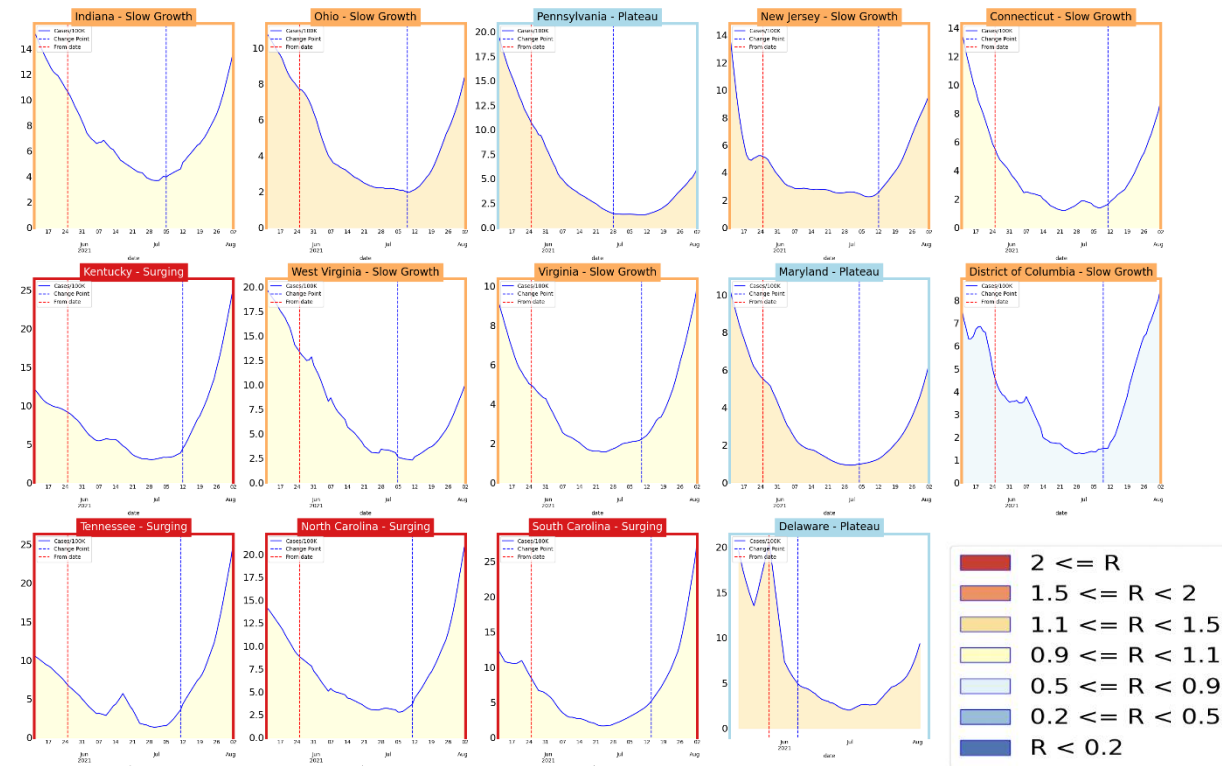
Other State Comparisons

Trajectories of States



- Surges expand further
 - Some limited signs of slowing in Missouri and Arkansas
 - Nearly half of jurisdictions in Surge (26) with Slow Growth (15) and Plateau (13) nearly evenly split
- 

Virginia and her neighbors



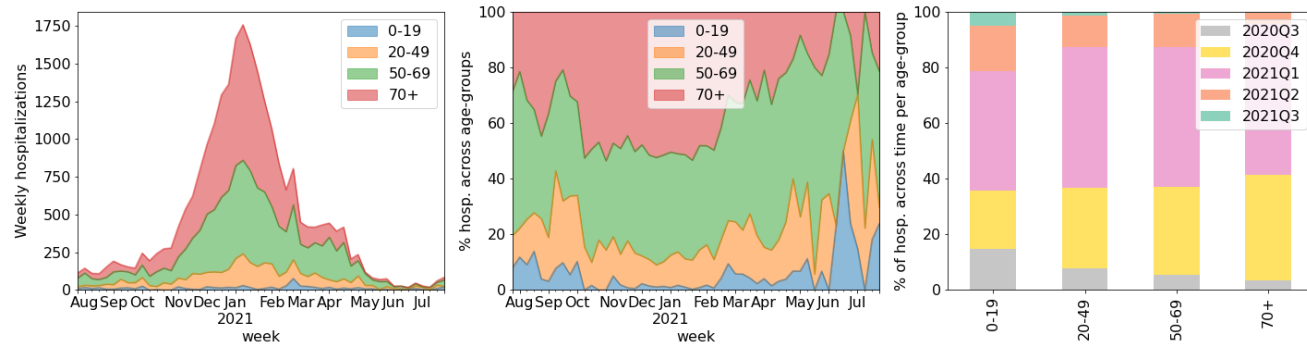
- All neighbors show upward trends
- Many neighbors are in surge and/or now have case rates above 20/100K

Hospitalizations across the US

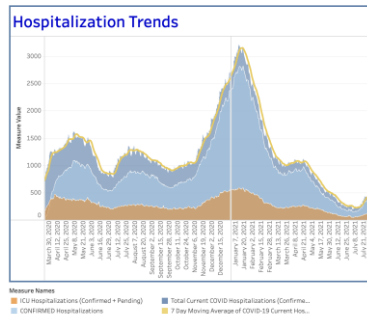
Hospitalization rates remain low in VA but rapid change is possible as seen in other states

- Hotspot states see rapid rise in hospitalizations especially among the younger age groups
- Hospitalization data is lagged and is current as of July 23

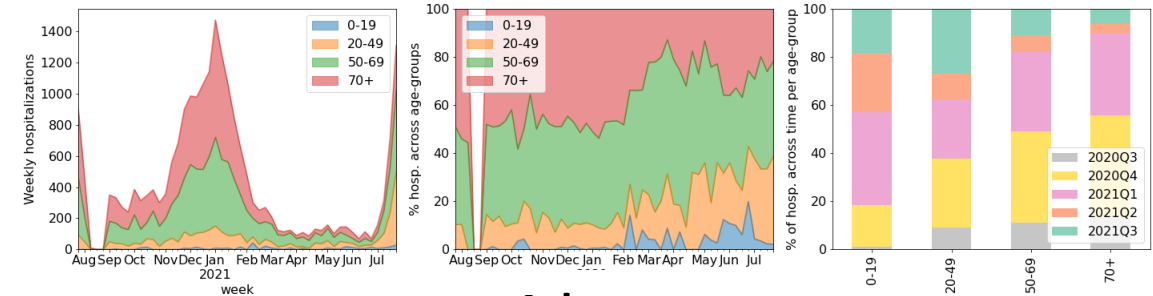
Virginia



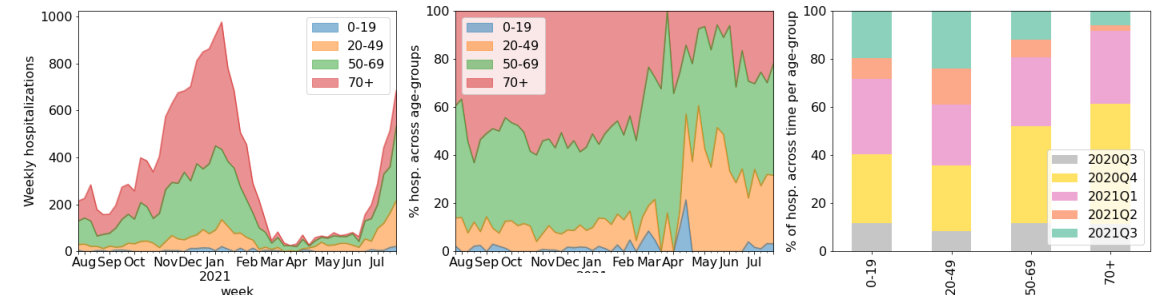
COVID-19 in Virginia Hospitals
As of: August 3, 2021



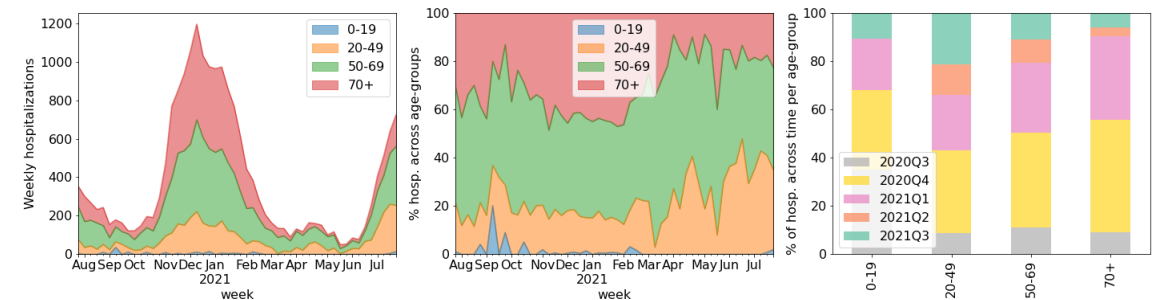
Louisiana



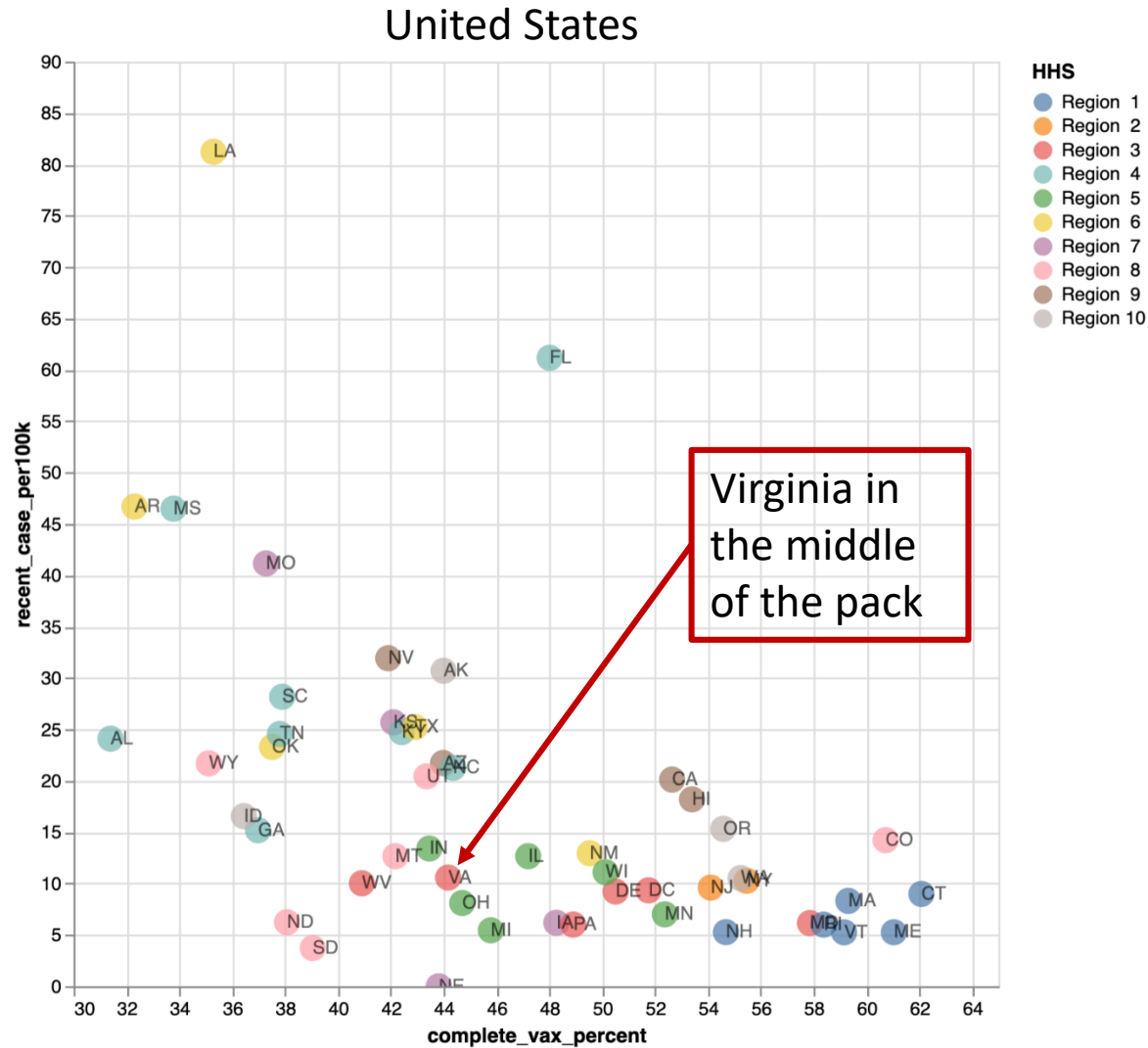
Arkansas



Nevada

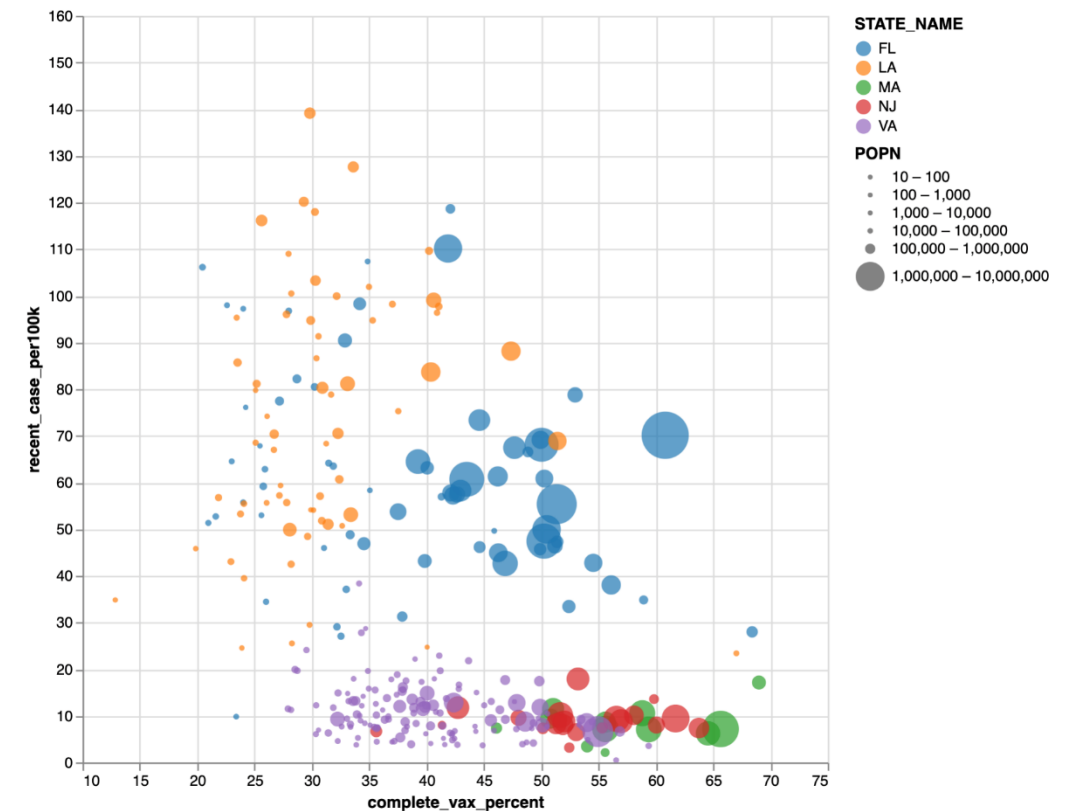


Recent Cases Correlate with Vax Coverage

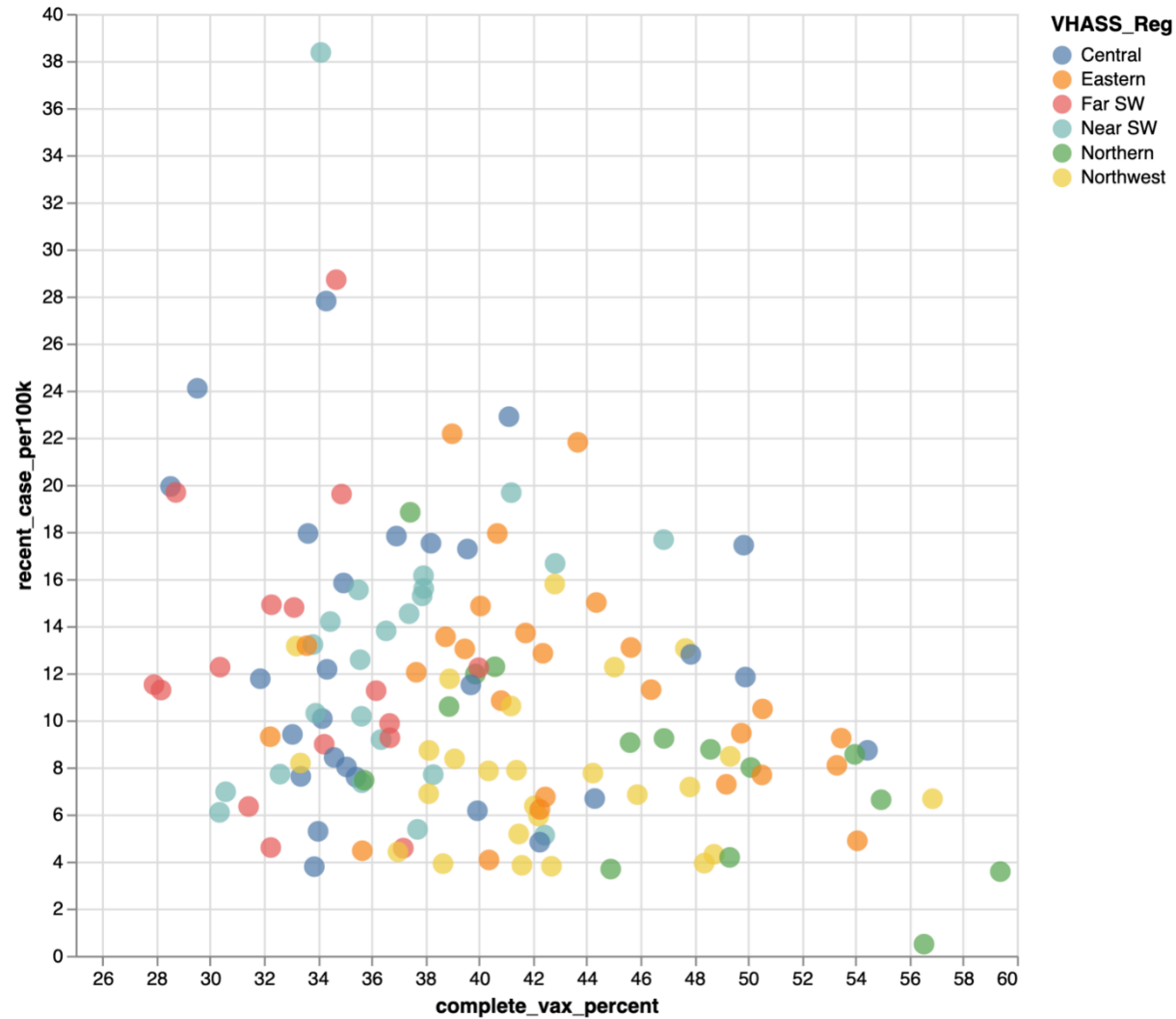


Mean cases per 100K vs. vaccination coverage

- Reasonable correlation at state level but quite a few outliers at sub-state level



Recent Cases Correlate Low Vax in VA counties



Mean cases per 100K vs. vaccinations for Virginia Counties

- Counties with higher vax coverage are maintaining lower case rates
- Many counties with low vax coverage continue to enjoy low case rates as well, though this may not hold

Model Update – Adaptive Fitting

Using Ensemble Model to Guide Projections

Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

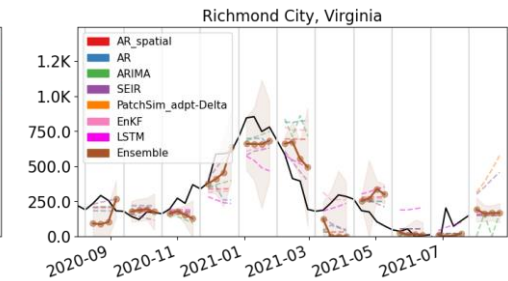
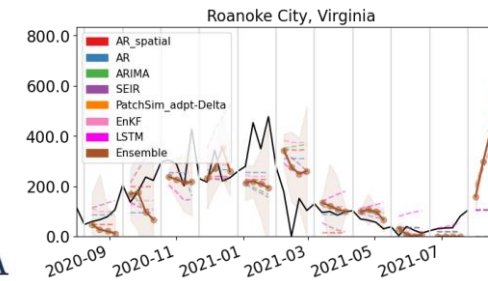
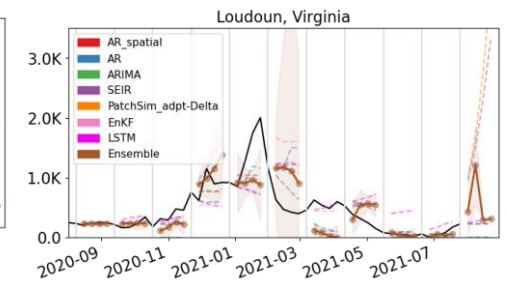
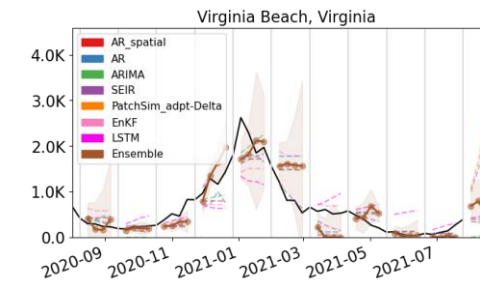
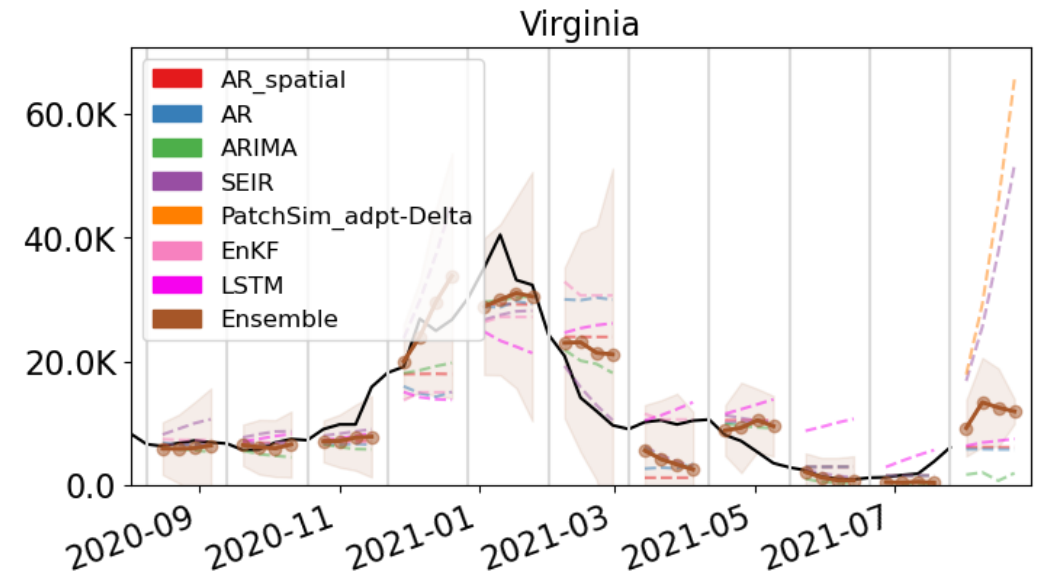
- Autoregressive (AR, ARIMA)
- Neural networks (LSTM)
- Kalman filtering (EnKF)

Weekly forecasts done at county level.

Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

Ensemble forecast provides additional 'surveillance' for making scenario-based projections.

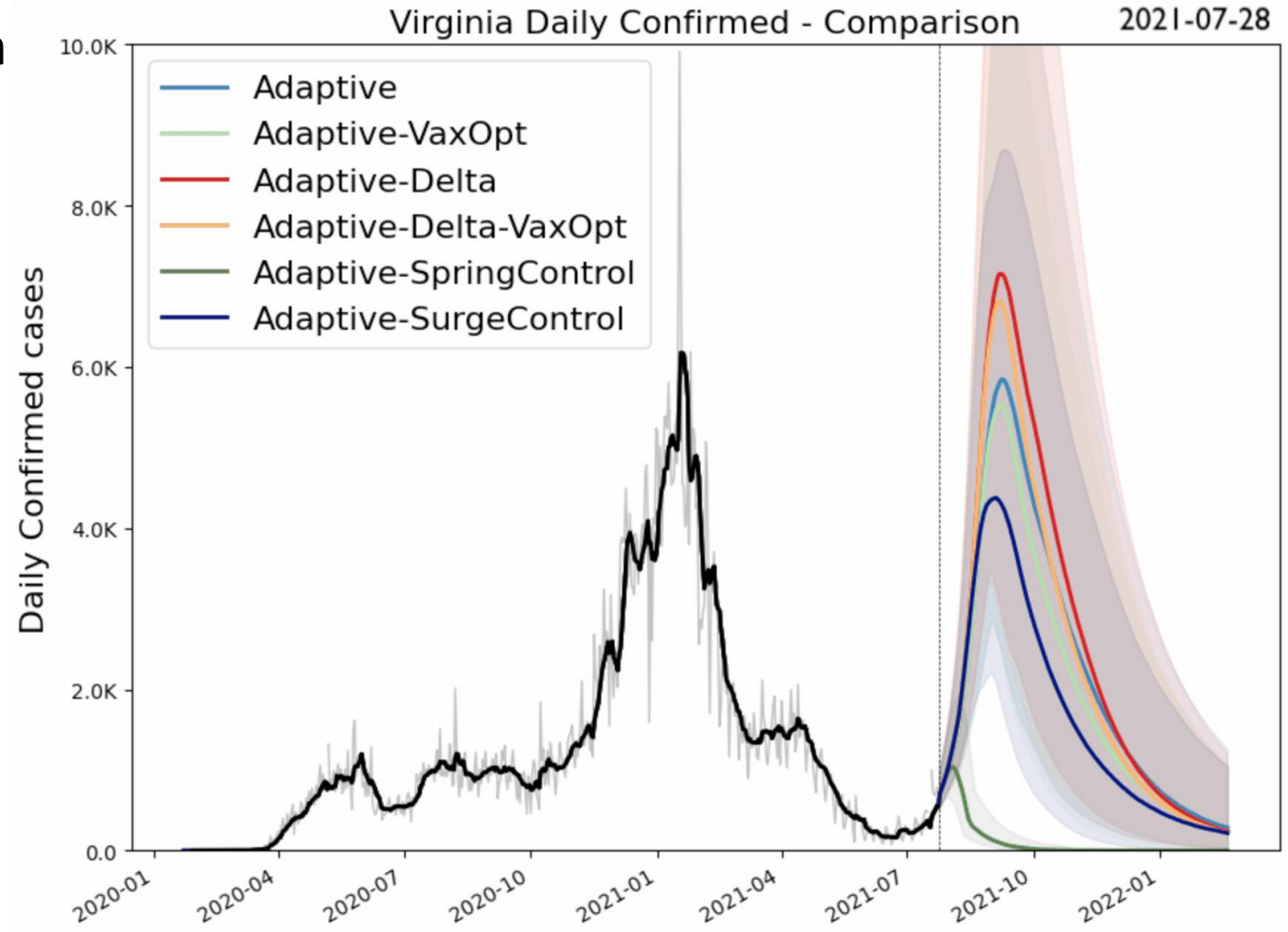
Also submitted to CDC Forecast Hub.



Model Assessment

Spot check of last week's projection

- This week's projection doesn't change much compared to last week's
- Last week's projection aligned well with



Delta Severity Suggestive Evidence

Table S1: Numbers of individuals testing positive (1 April to 6 June 2021) and number admitted to hospital from the community within 14 days of testing positive from the EAVE II cohort

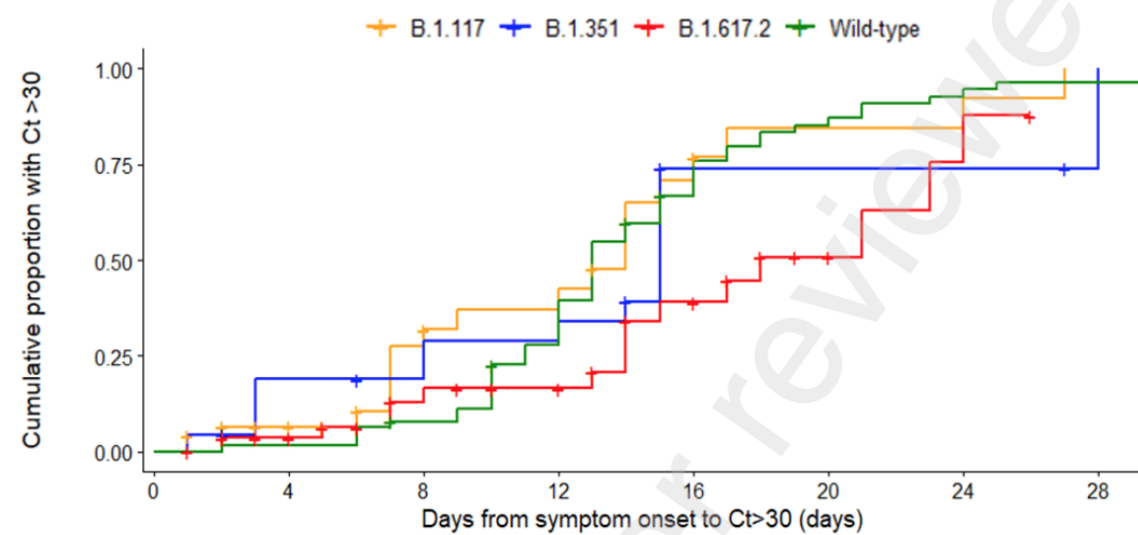
S Gene	Person Years Exposure	N	Number Admitted to Hospital	Rate per 100 person years
S Gene Negative	615.2	9996	223	36.2
S Gene Positive	214.7	7723	134	62.4
Weak S Positive	97.6	1824	20	20.5

N – Number of individuals testing positive

In a recent study 97% of S gene positive cases sequenced in Scotland were the Delta variant and that 99% of Delta variants were S gene positive. Found that S gene-positive cases were associated with an **increased risk of COVID-19 hospital admission: hazard ratio (HR) 1.85 (95% CI 1.39–2.47)** when compared to S gene-negative cases

<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2901358-1>

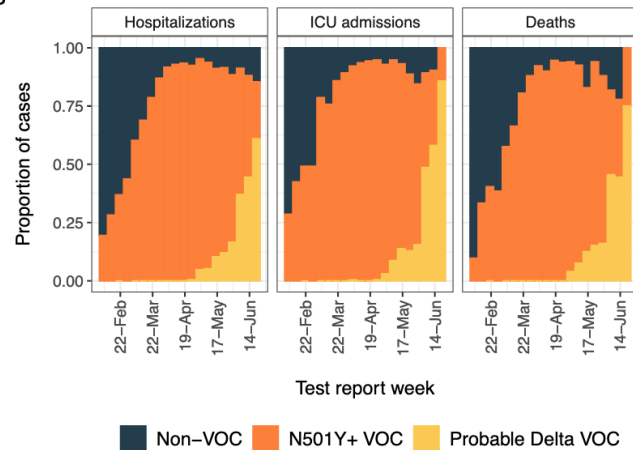
S Gene Negative are mostly Alpha
S Gene Positive are mostly Delta



838 VOC infections in Singapore in the study period. After adjusting for age and gender, **B.1.617.2 infection was associated with higher odds of oxygen requirement, ICU admission, or death (adjusted odds ratio (aOR) 4.90, [95% CI 1.43-30.78])**. B.1.617.2 was associated with significantly lower PCR Ct values and significantly longer duration of Ct value ≤ 30 (estimated median duration 18 days for B.1.617.2, 13 days for wild-type).

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3861566

B

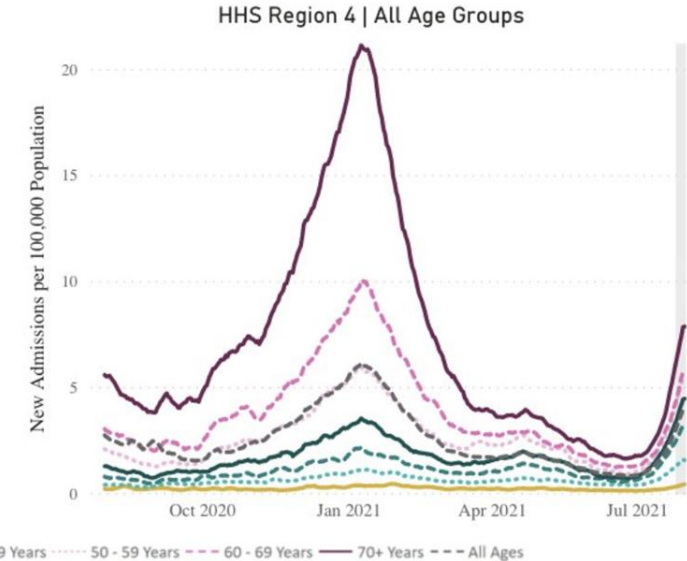
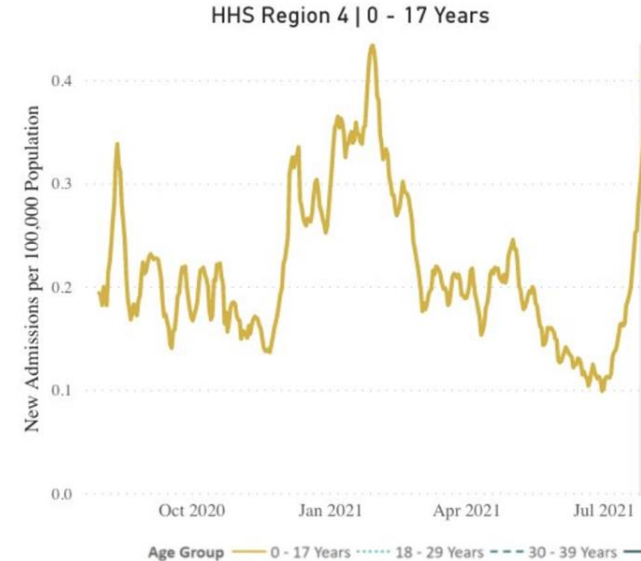


Study of infections in Ontario Feb. to June 2021 showed **increases with Delta variant were more pronounced: 120% (93-153%) for hospitalization; 287% (198-399%) for ICU admission; and 137% (50-230%) for death.**

<https://www.medrxiv.org/content/10.1101/2021.07.05.21260050v2>

Similar to trend seen in Scotland, more severe outcomes in unvaccinated youth

<https://twitter.com/cmeyeaton/status/1422624128918556684>



Key Takeaways

Projecting future cases precisely is impossible and unnecessary.

Even without perfect projections, we can confidently draw conclusions:

- **Case rates in Virginia continue to rise quickly amidst a background of surges across the nation**
- VA mean weekly incidence up to 14/100K from 7.8/100K, US up to 25/100K (from 15.6/100K)
- Vaccination rates continue rebound while acceptance among the unvaccinated ticks up and mask usage also increases slightly
- Uncertainty around severity of Delta variant remains, however, the experience of other states / countries suggest potential for higher severity
- Recent updates:
 - Analysis of mask use, reasons by vax acceptance level
 - Deeper dive on Delta variant severity
- The situation continues to change. Models continue to be updated regularly.

Questions?

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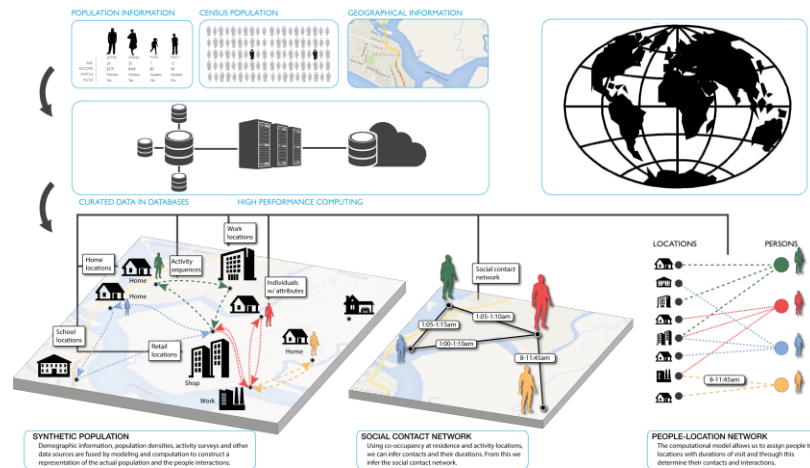
Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Jiangzhuo Chen, Clark Cucinell, Patrick Corbett, Allan Dickerman, Stephen Eubank, Stefan Hoops, Ben Hurt, Ron Kenyon, Brian Klahn, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie

Supplemental Slides

Agent-based Model (ABM)

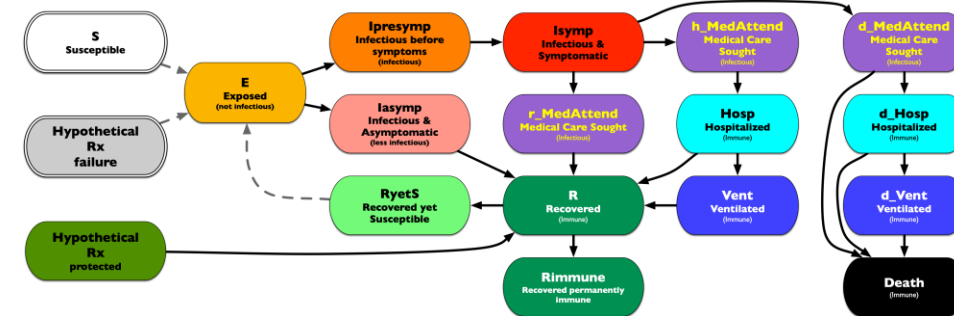
EpiHiper: Distributed network-based stochastic disease transmission simulations

- Assess the impact on transmission under different conditions
- Assess the impacts of contact tracing



Synthetic Population

- Census derived age and household structure
- Time-Use survey driven activities at appropriate locations



Detailed Disease Course of COVID-19

- Literature based probabilities of outcomes with appropriate delays
- Varying levels of infectiousness
- Hypothetical treatments for future developments